Methodologies and Applications of Geminal Bis(boronic) Esters

Author: Xun Liu

Boston College

The Graduate School of Arts and Sciences

Department of Chemistry

METHODOLOGIES AND APPLICATIONS OF GEMINAL BIS(BORONIC) ESTERS

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XUN LIU

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Dissertation Advisor:

Professor James P. Morken

ABSTRACT: 1,1-Bis(boronic) esters have attracted significant attention these days due to their unique reactivity. In this thesis, I will show that readily available reagents can undergo deborylative alkylation to deliver synthetically useful primary, secondary and tertiary boronic esters. 1,1-Diboryl alkanes can also engage in base-promoted deborylative cyclization to afford diversified cyclopentane rings with boron motifs attached. This transformation is very appealing because of the prevalence of five-membered rings in natural products. Lastly, it will be showed that geminal bis(boronic) esters can act as an important cornerstone in constructing relatively complicated structures such as natural product Arenolide.

Dedicated to:

My parents, who love and support me unconditionally

ACKNOWLEDGEMENTS

First of all, I would like to thank my advisor Professor James Morken. He is extremely brilliant, knowledgeable and talented, while at the same time, being so hardworking, humble and kind-hearted. He is my role model and I was lucky to be able to learn from him. Without his patient guidance, I could not accomplish my dream of being a scientist. Whenever I needed help, his door was always open to me. I owe a great debt of gratitude to him. I would like to thank Professor Amir Hoveyda for always being supportive, and for serving as my thesis committee member and referee. You are like a second advisor to me. I would also like to thank Professor Jeffery Byers for serving as my committee member and reading my thesis, it is always a pleasure to hear your insightful opinions about chemistry. Max, thank you very much for your hard work, kind help and humor. It was a joy working with you and I learned a lot from you. Chunrui, thank you very much for guiding me when I was a junior graduate student, your wisdom and passion for chemistry inspired me everyday. Kai, thank you so much for carrying me through my challenging first year, you were so patient with me and I could not have asked for a better mentor. I would also like to thank MJ, Adam, Yong and Marshall for proofreading my thesis. I am also grateful to have had the opportunity to learn from Lichao, Jason, Miao, Senmiao and Zhiyong, all of whom are smart and inspiring. Jiachen, Hanlu and Xin, thank you so much for your friendship and for making my journey to

become a scientist more joyful. Last but not least, I would like to thank my parents for being incredibly supportive and allowing me to soar and pursue my dreams.

TABLE OF CONTENTS

List of Abbreviations

Å: angstrom

Ac: acetate

Ar: aryl

acac: acetylacetone

aq: aqueous

$B_2(cat)_2$: bis(catecholato)diboron

$B_2(pin)_2$: bis(pinacolato)diboron

BBD: borabicyclo[3.3.2]decanes

BBN: borabicyclo[3.3.1]nonane

BINOL: binaphthol

Bn: benzyl

Boc: *tert*-butoxycarbonyl

Boc_2O: di-*tert*-butyldicarbonate

Bz: benzoyl

cat: catechol

cod: cyclooctadiene

COSY: correlation spectroscopy

Cy: cyclohexyl

DART: direct analysis in real time

dba: dibenzylidene acetone

DCM: dichloromethane

DFT: density functional theory

DIBAL-H: di-*iso*-butylaluminum hydride

DMAP: 4-dimethylaminopyridine

DMF: dimethylformamide

dppe: 1,2-bis(diphenylphosphino)ethane

dppf: 1,1'-bis(diphenylphosphino)

ferrocene

dppp: 1,3-bis(diphenylphosphino)propane

dr: diastereomeric ratio

ee: enantiomeric excess

eq: equation

equiv: equivalent(s)

er: enantiomeric ratio

ESI: electrospray ionization

Et_2O: diethyl ether

EtOAc: ethyl acetate

GLC: gas liquid chromatography

h: hour(s)

HPLC: high performance liquid chromatography

HRMS: high resolution mass spectrometry

Ipc: *iso*-pinocampheyl

IR: infrared spectroscopy

L: ligand

LG: leaving group

LiHMDS: lithium bis(trimethylsilyl) amide

M: molar or metal

NaHMDS: sodium bis(trimethylsilyl) amide

NHC: *N*-heterocyclic carbene

NMO: 4-methylmorpholine *N*-oxide

NMR: nuclear magnetic resonance

NOESY: nuclear overhauser effect spectroscopy

Nu: nucleophile

Ph: phenyl

pin: pinacol

PMA: phosphomolybdic acid

QUINAP: 1-(2-diphenylphosphino-1-naphthyl)isoquinoline

rt: room temperature

SFC: supercritical fluid chromatography

SiO_2: silica gel

TADDOL: (4*R*,5*R*)-(–)-2,2-dimethyl-α, α, α', α',-tetraphenyl-1,3-dioxolane-4,5-dimethanol

TBDPS: *tert*-butyldiphenylsilyl

TBME: *tert*-butyl methyl ether

TBS: *tert*-butyldimethylsilyl

TEMPO: 2,2,6,6-Tetramethyl-1-piperidi-nyloxy

Tf: trifluoromethanesulfonyl

TFA: trifluoroacetyl

THF: tetrahydrofuran

TMEDA: tetramethylethylenediamine

TMSCl: trimethylsilyl chloride

TPAP: tetrapropylammonium perruthenate

TS: transition state

Xantphos: 4,5-Bis(diphenylphosphino)-9, 9-dimethylxanthene

Chapter 1

Development of 1,1-Bis(boronic) Esters and Their Transformations

1.1 Introduction

Transformations of geminal bis(boronic) esters have been studied intensively during the past decade, and the product boronic esters obtained from these methodologies are of great synthetically value.[1] Boronic esters can be converted into various functional groups such as alcohols,[2] amines,[3] and halides[4] in a stereorententive fashion. In this chapter, a short review about the past and present methods that involved geminal bis(boronic) esters will be presented.

1.2 Development of 1,1-Bis(boronic) Esters and Their Transformations

The chemistry of geminal bis(borane) can be dated back to 1966, when Zweifel and coworkers[5] revealed that the terminal alkyne **1.1** could undergo hydroboration

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[1] Hall, D. G. *Boronic Acids*, 2nd ed.; Wiley-VCH: Weinheim, **2011**.

[2] Brown, H. C.; Snyder, C.; Subba Rao, B. C.; Zweifel, G. *Tetrahedron* **1986**, *42*, 5505-5510.

[3] Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449-16451.

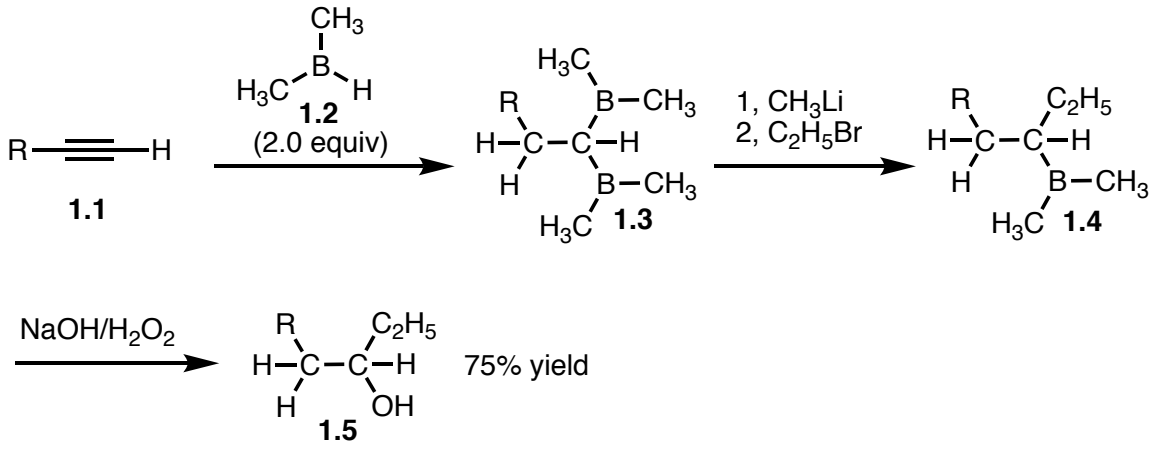
[4] Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2011**, *133,* 16794-16797.

[5] Zweifel, G.; Arzoumanian, H. *Tetrahedron Lett.* **1966**, 2535-2538.

consecutively with dimethyl borane **1.2** to afford 1,1-diboryl alkane **1.3**. After treating diboryl compound **1.3** with methyl lithium and trapping with bromoethane, the deborylative alkylated product was furnished, which was then oxidized to the corresponding alcohol **1.5** in good yield (Scheme 1.1).

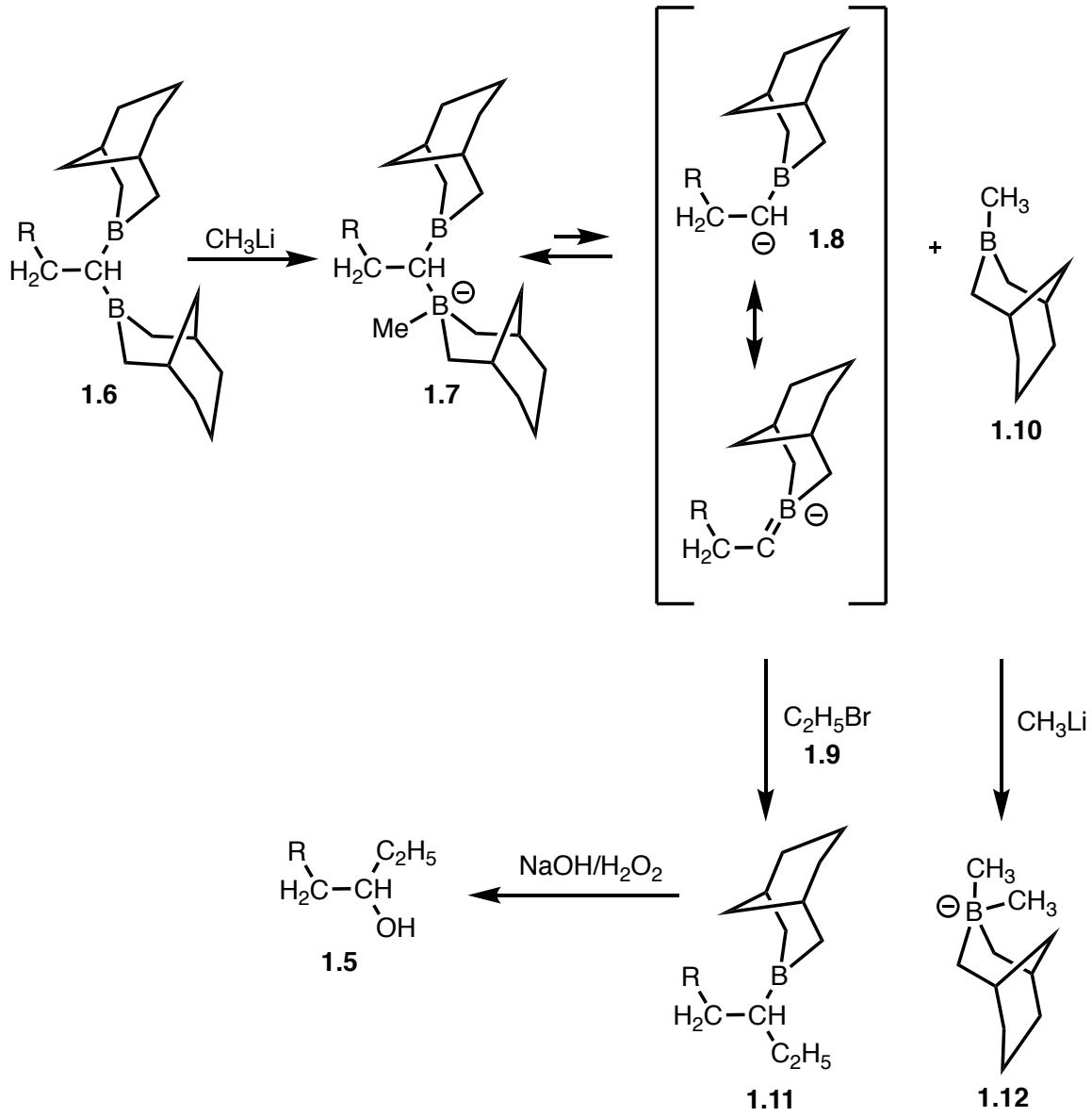
Zweifel proposed a possible mechanism for this transformation based on ^{1}H NMR studies (Scheme 1.2).[6] They observed a resonance at high field with chemical shift -0.7 ppm, which proposed to be the ate complexes **1.7** and **1.12**. After bromoethane was added, this peak at -0.7 ppm decreased by 85%. This observation was consistent with the scenario that the generated carbonanion **1.8** (in resonance with borate alkene structure) further reacted with bromoethane to afford the alkylated product **1.11**; while ate complex **1.12** was unreactive towards bromoethane, which accounted for the residual signal peak at -0.7 ppm.

Scheme 1.1 Intermolecular Alkylation with 1,1-Diboryl Alkane



[6] Zweifel, G.; Fisher, R. P.; Horng, A. *Synthesis* **1973**, 37-38.

Scheme 1.2 Mechanism for Deborylative Alkylation Reaction

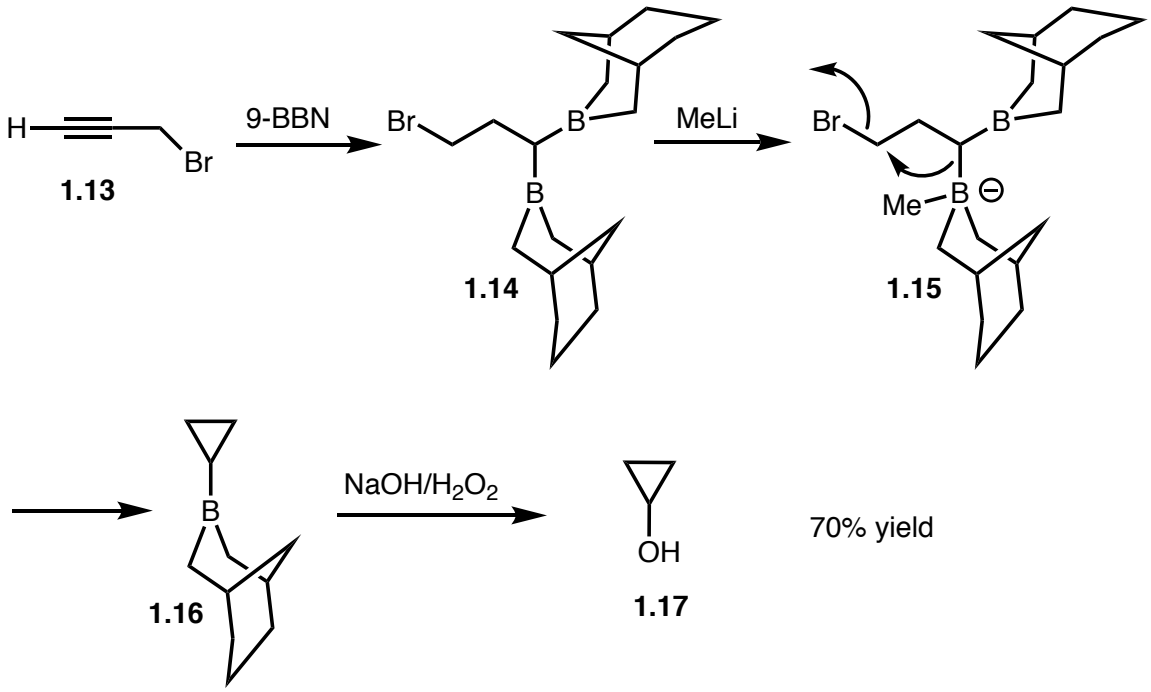


In 1969, Brown and coworkers developed an interesting intramolecular transformation of these 1,1-diboryl compounds (Scheme 1.3).[7] The geminal bis(boranes)

[7] Brown, H. C.; Rhodes, S. P. *J. Am. Chem. Soc*. **1969**, *91*, 4306-4307.

1.14 bearing a bromide leaving group was treated with methyl lithium to generate boronate **1.15**, which could then react with the electrophilic halide to form three-membered ring product **1.16** with a synthetically useful borane motif still appended.

Scheme 1.3 Intramolecular Alkylation with 1,1-Diboryl Alkane



Subsequent to these early reports with boranes, Matteson and co-workers[8] disclosed a route to synthesize geminal bis(boronic) ester **1.19**. After treating trimethyl borate **1.18** with lithium metal and dichloromethane at -30 ^{o}C in THF, the desired product diboronic ester **1.19** could be obtained. Although the yield was low for this route, it nonetheless provided material to study.

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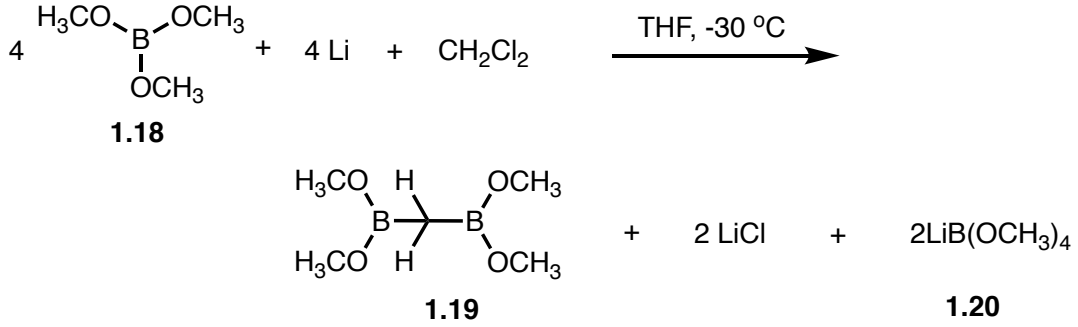
[8] Castle, R. B.; Matteson, D. S. *J. Organomet. Chem.* **1969**, *20*, 19-28.

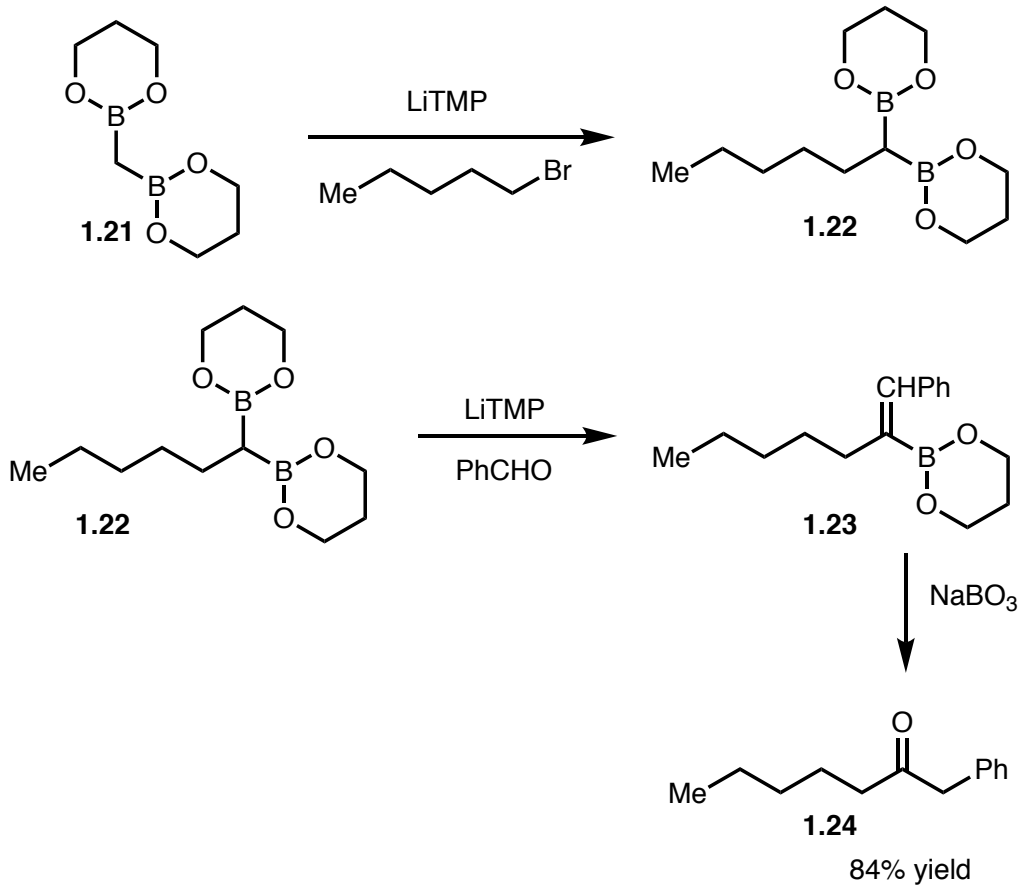
Scheme 1.4 Matteson's Method to Synthesize Geminal Bis(boronate)



With the 1,1-diboryl methane **1.21** obtained on large scale, Matteson explored its applications.[9] First, they found that a bulky base such as lithium tetramethylpiperidide (LiTMP) could deprotonate the acidic α-H of 1,1-diboryl methane **1.21**, and the resulting anion would then react with 1-bromopentane to afford the substituted geminal bis(boronate) **1.22**. Second, the α-H of the carbon in compound **1.22** could be deprotonated again, and subsequent reaction with benzaldehyde delivered vinyl boronate **1.23**. After being oxidized into an alcohol, the tautomeric product ketone **1.24** was obtained in 84% yield.

[9] Matteson, D. S.; Moody, R. J. *Organometallics*, **1982**, *1*, 20-28.

Scheme 1.5 Further Transformations of Geminal Bis(boronate) **1.21**

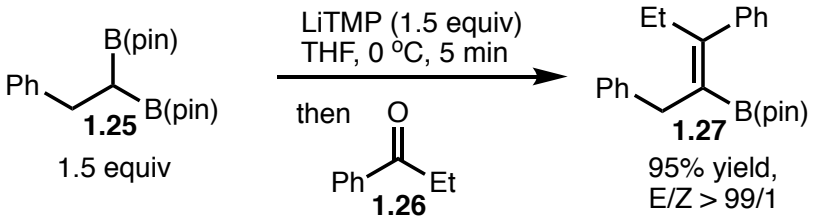


The chemistry of geminal bis(boranates) had been rarely visited for several decades until 2010, when Shibata and Endo[10] reported a boron-Wittig reaction in which 1,1-organoboronates **1.25** could undergo nucleophilic addition to ketones after deprotonation with LiTMP. This furnished tetra-substituted alkenyl boronic esters, which were proven to be useful building blocks because they could readily cross couple with

[10] Endo, K.; Hirokami, M.; Shibata, T. *J. Org. Chem.* **2010**, *75*, 3469-3472.

aryl electrophiles for further functionalization, as demonstrated by the synthesis of Tamoxifen derivatives. (Scheme 1.6)

Scheme 1.6 Boron Wittig Reaction Starting from 1,1-Organoboronate Compound **1.25**



In the same year, Shibata and Endo[11] also reported that geminal bis(boronic) esters bearing an sp^3-hybridized carbon could undergo cross-coupling reaction with aryl halides at room temperature. This reaction occurred with high chemoselectively to afford mono-substituted boronic ester **1.30** in a racemic form. Notably, the reaction would not undergo further Suzuki coupling reaction. A set of mechanistic studies using boron NMR was carried out, which revealed that a boron ate complex was the reactive intermediate.

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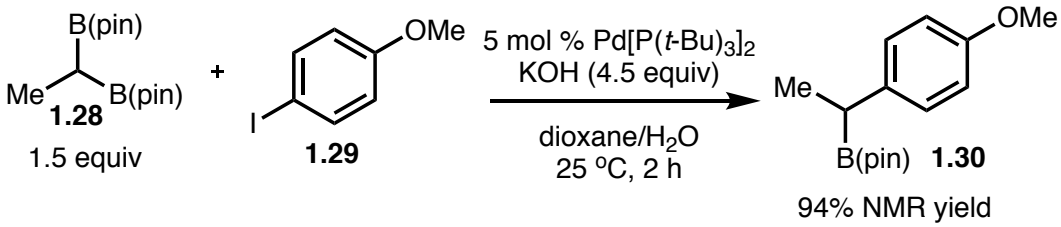
[11] Endo, K.; Ohkubo, T.; Hirokami, M.; Shibata, T. *J. Am. Chem. Soc.* **2010**, *132*, 11033-11035.

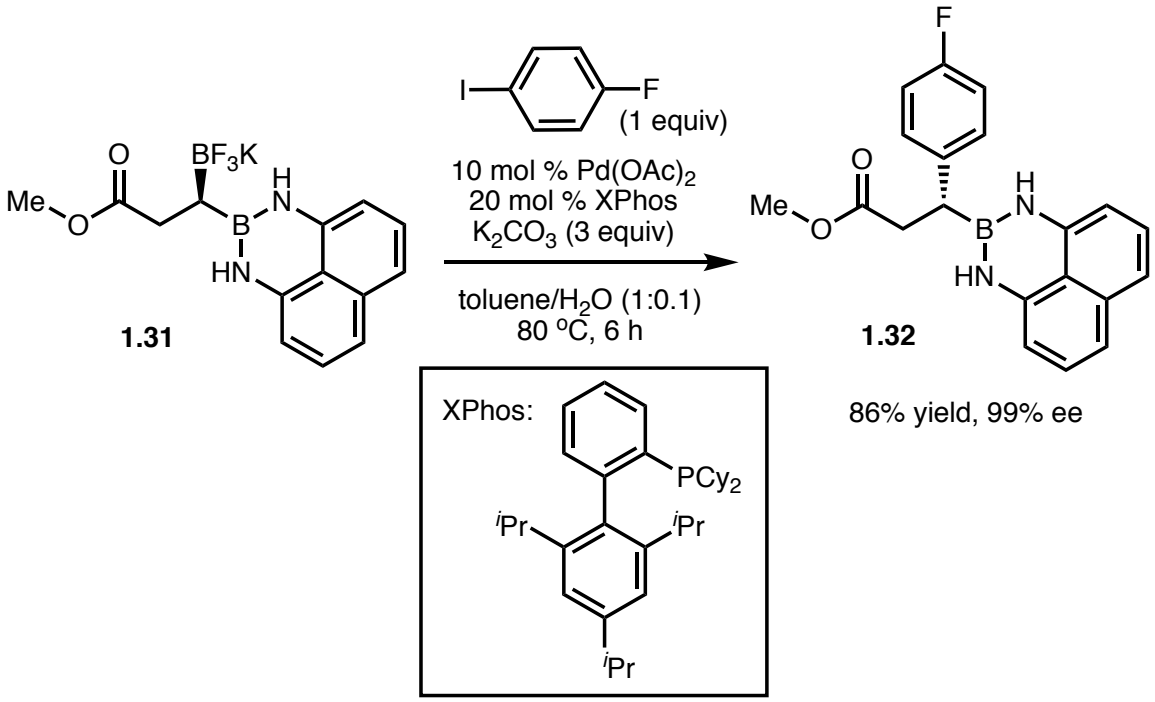
Scheme 1.7 Pd-Catalyzed Suzuki Coupling between 1,1-Diboryl Alkanes and Aryl Halides



In 2013, Hall and coworkers[12] disclosed a stereospecific Suzuki coupling reaction between enantioenriched 1,1-diboryl alkane **1.31** and 4-fluoroiodobenzene to furnish a stereocenter-inverted product **1.32**. Through the study of the corresponding X-ray structure, they reasoned that the lone pairs of electrons from the carbonyl oxygen might donate to the empty p orbital of the adjacent boronic acid, which could facilitate the transmetallation step. In addition, stabilization of the intermediate alkylpallladium species by the B(dan) moiety made it possible to accomplish the Suzuki coupling reaction efficiently.

[12] Lee, J. C. H.; McDonald, R.; Hall, D. G. *Nat. Chem.* **2011**, *3*, 894-899.

Scheme 1.8 Stereospecific Suzuki Coupling between Geminal Bis(boronate) Ester and Aryl Halides



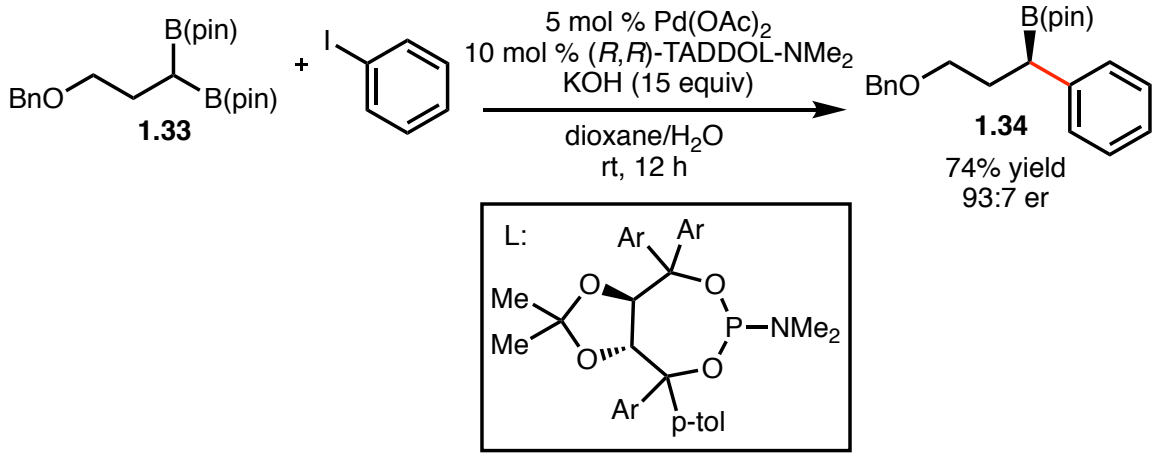
In 2014, our group[13] developed an enantioselective version of the Suzuki coupling reaction between 1,1-diboryl alkane **1.33** and aryl halides to furnish mono-substituted boronic ester **1.34** in a good yield with high enantioselectivity. Later, the electrophiles for the coupling reaction were extended from aryl halides to tri-substituted vinyl halides by switching the chiral ligand from a phosphoramidite to a Josiphos derivative.[14]

---

[13] Sun, C.; Porter, B.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 6534-6537.

[14] Potter, B.; Szymaniak, A. A.; Edelstein, E. K.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 17918-17921.

Scheme 1.9 Pd-Catalyzed Enantioselective Suzuki Coupling between Geminal Bisboronate and Aryl Halides



In 2015, Meek and coworkers[15] demonstrated that copper complexes could catalyze the nucleophilic addition of substituted geminal bis(boronate) derivative to aryl/vinyl aldehydes in the presence of a chiral monodentate phosphoramidite ligand, delivering the *syn*-1,2-hydroxyboronates with excellent control of both enantio- and diastereoselectivity. The enantioeneriched mono boronic ester compound could be easily converted into *syn*-1,2 diol product **1.35** upon oxidative workup (Scheme 1.10).

Later, Meek found that silver (I) acetate[16] could also catalyze the 1,2-nucleophilic addition of geminal bis(boronic) ester **1.33** to aldehydes (Scheme 1.11). However, in contrast to the copper-catalyzed reaction, the adjacent hydroxyl group and

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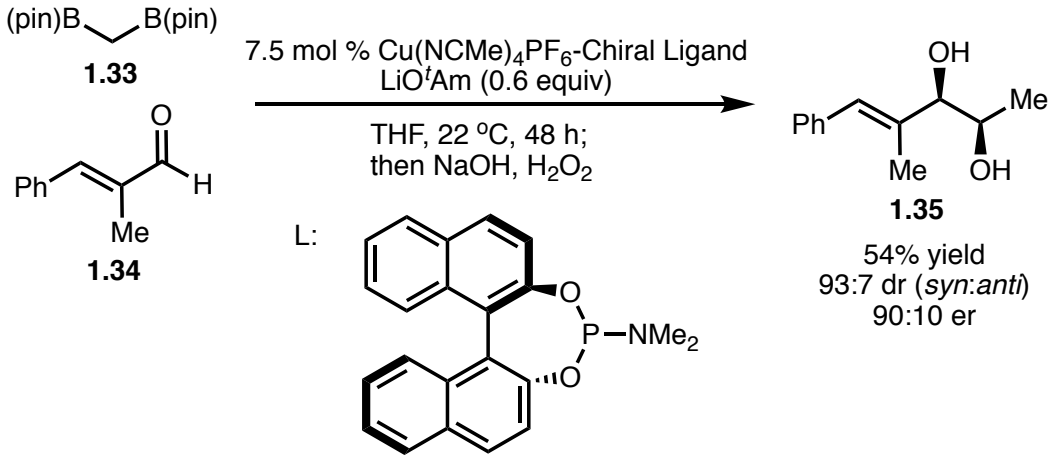
[15] Joannou, M. V.; Moyer, B. S.; Meek, S. J. *J. Am. Chem. Soc.* **2015**, *137,* 6176-6179.

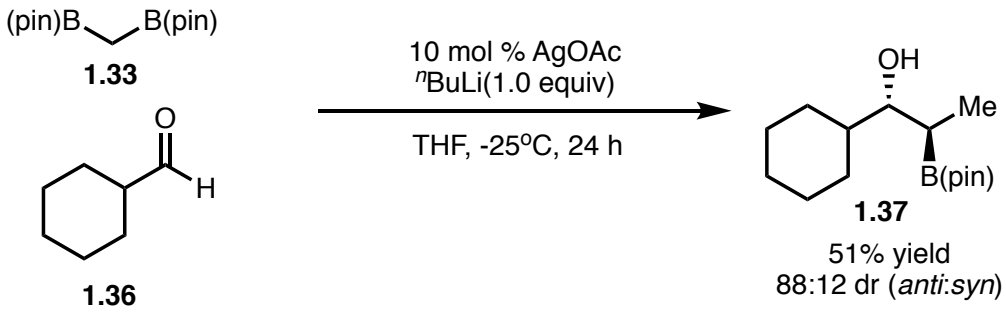
[16] Joannou, M. V.; Moyer, B. S.; Goldfogel, M. J.; Meek, S. J. *Angew. Chem. Int. Ed.* **2015**, *54*, 14141-14145.

boryl group were installed with *anti*-stereoselectivity **1.37**. Notably, different aldehydes including aryl, alkenyl and alkyl aldehydes were all suitable electrophiles.

Scheme 1.10 Copper-Catalyzed 1,2-Addition of 1,1-Diboryl Alkanes to Aldehydes



Scheme 1.11 Silver-Catalyzed 1,2-Addition of 1,1-Diboryl Alkanes to Aldehydes



While only a few reports had shown reaction between geminal bis(boronate) **1.33** and allyl electrophiles,[17] Hoveyda and coworkers[18] reported an elegant copper-catalyzed enantioselective allylic substitution reaction by using sulfonate-containing chiral NHC as ligand (Scheme 1.12). They found that the more Lewis acidic the metal salt was, the higher ratio of branched products they obtained. Applying this methodology, they constructed branched homoallylic boronic ester **1.39** in good yield with excellent enantioselectivity, which was further elaborated into the natural product rhopaloic acid A.

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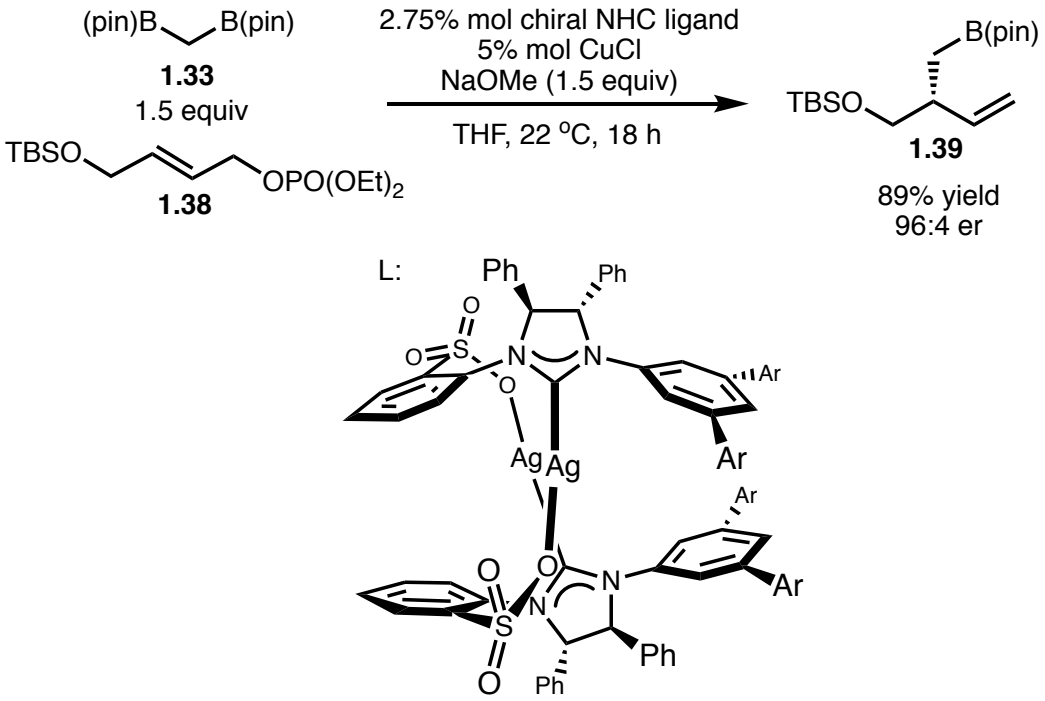
[17] (a) Endo, K.; Ohkubo, T.; Ishioka, T.; Shibata, T. *J. Org. Chem*. **2012**, *77*, 4826-4831. (b) Kim, J.; Park, S.; Park, J.; Cho, S. H. *Angew. Chem. Int. Ed.* **2016**, *55*, 1498-1501. (c) Zhan, M.; Li, R.-Z.; Mou, Z.-D.; Cao, C.-G.; Liu, J.; Chen, Y.- W.; Niu, D. *ACS Catal.* **2016**, *6*, 3381-3386. (d) Zhang, Z.-Q.; Zhang, B.; Lu, X.; Liu, J.-H.; Lu, X.-Y.; Xiao, B.; Fu, Y. *Org. Lett.* **2016**, *18*, 952-955.

[18] Shi, Y.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2016**, *55*, 3455-3458.

Scheme 1.12 Cu/NHC-Catalyzed Allylic Substitution Reaction of Geminal Bis(boronate)



In 2016, Cho and coworkers[19] reported that 1,1-diboryl methane **1.33** could add to Ellman's aldimines[20] in a highly diastereoselective manner under the catalysis of copper bromide and a bidentate phosphine ligand. This was a beautiful design because without copper as the catalyst, the 1,2-addition reaction usually suffered from low diastereoselectivities. The resulting primary boronic ester product could then be oxidized into a protected 1,2-amino alcohol (Scheme 1.13).

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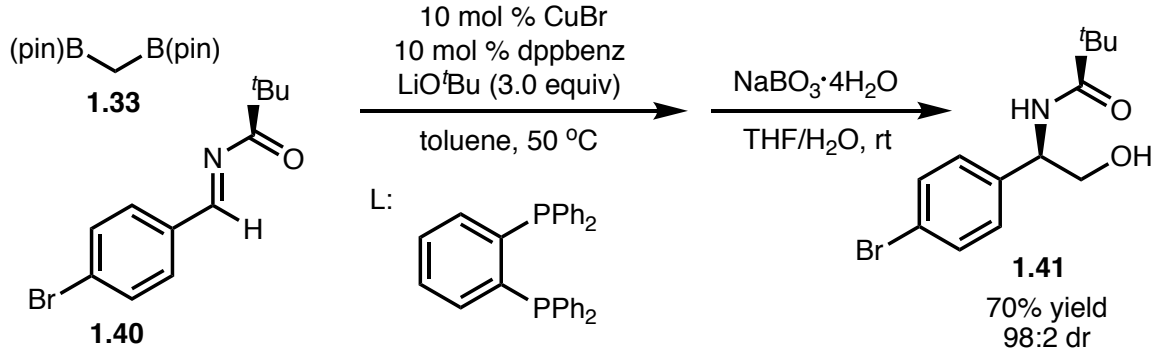
[19] Park, J.; Lee, Y.; Kim, J.; Cho, S. H. *Org. Lett.* **2016**, *18*, 1210-1213.

[20] Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600-3740.

Scheme 1.13 Copper Catalyzed 1,2 Addition of Geminal Bis(Boronate) to Ellman's Imine

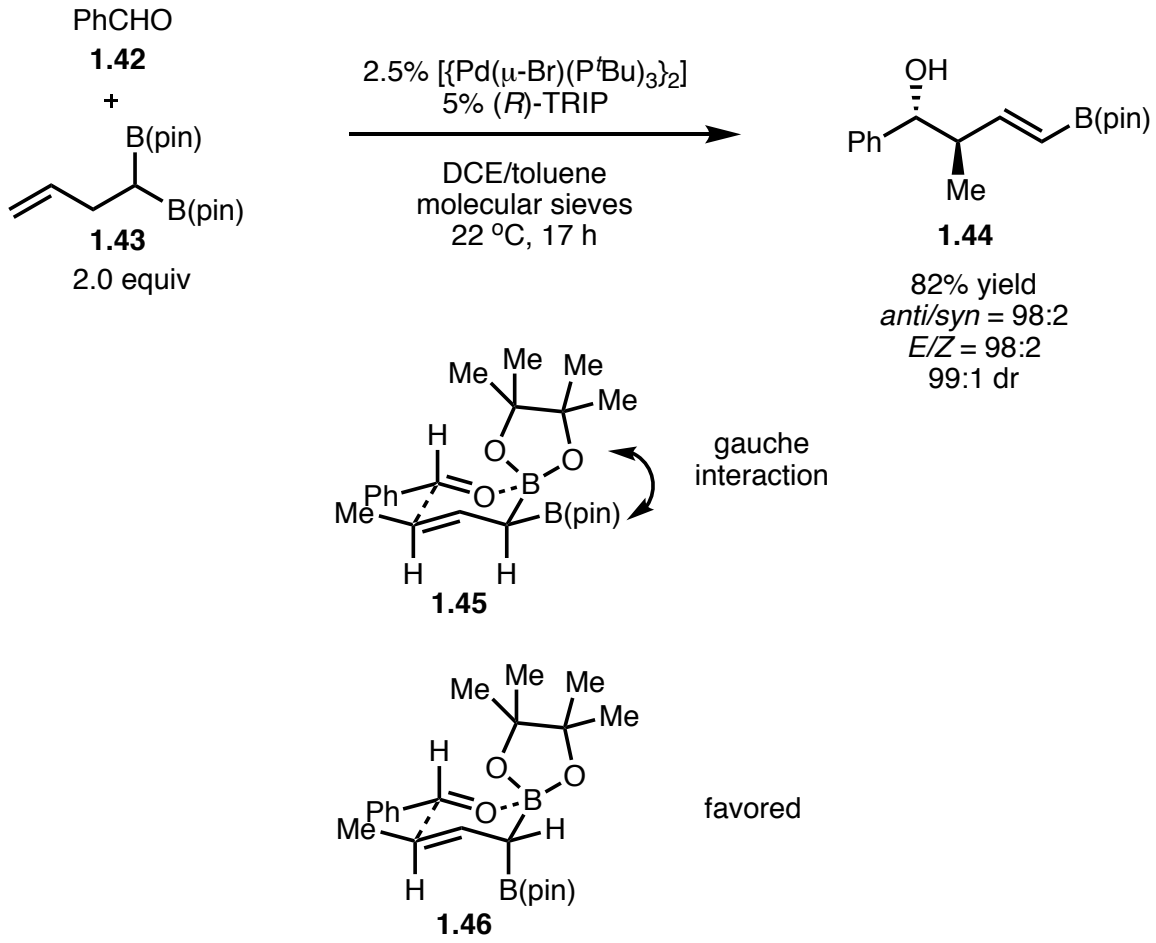


Earlier this year, Murakami and coworkers[21] reported that 1,1-diborylalk-3-ene could undergo palladium-catalyzed alkene transposition, followed by allylation reaction with aldehydes in the presence of a chiral phosphoric acid, to afford (*Z*)-*δ*-boryl-substituted *anti*-homoallylic alcohols (Scheme 1.14). This *Z*-alkene was then isomerized into the *E* configuration by a palladium catalyst. Mechanistic studies suggested the major product was generated from the transposed (*E*)-1,1-diborylalk-2-ene, which was more reactive compared to (*Z*)-1,1-diborylalk-2-ene. The authors proposed that a gauche interaction between geminal bis(boronic) ester **1.46** in the six-membered cyclic transition state made the formation of (*E*)-*δ*-boryl-substituted product less favored, and thus resulted in the formation of (*Z*)-*δ*-boryl-substituted *anti*-homoallylic alcohol.

[21] Miura, T.; Nakahashi, J.; Murakami, M. *Angew. Chem., Int. Ed.* **2017**, *56*, 6989-6993.

The substrate scope of aldehydes was not limited to aromatic ones; but could also be expanded to aliphatic substrates.

Scheme 1.14 Enantioselective Synthesis of (*E*)-*δ*-Boryl-Substituted *anti*-Homoallylic Alcohols



1.3 Conclusions

In conclusion, geminal bis(boronic) esters can undergo a wide array of transformations to deliver diversified synthetically useful products. With the readily

accessibility of 1,1-diborylalkanes, useful new reactions of these compounds will emerge more and more in the foreseeable future.

Chapter 2

Development of Base-Promoted Deborylative Alkylation of 1,1-Bis(boronic) Esters

2.1 Introduction

Alkylboronic esters can undergo oxidation or amination to deliver synthetically valuable building blocks such as alcohols[1] or amines[2] in a stereoretentive fashion. Hence, development of synthetic routes to efficiently access alkylboronic esters is highly desirable. Traditionally, boronic esters could be obtained through hydroboration of alkenes with transition metal-based catalysts such as rhodium or iridium,[3] or even without a metal catalyst,[4] to afford the anti-Markovnikov products. The regioselectivity and enantioselectivity of these hydroboration transformations can be tuned with the appropriate combination of transition metal complex and ligands (Scheme 2.1).[5]

---

[1] Brown, H. C.; Snyder, C.; Subba Rao, B. C.; Zweifel, G. *Tetrahedron* **1986**, *42*, 5505-5510.

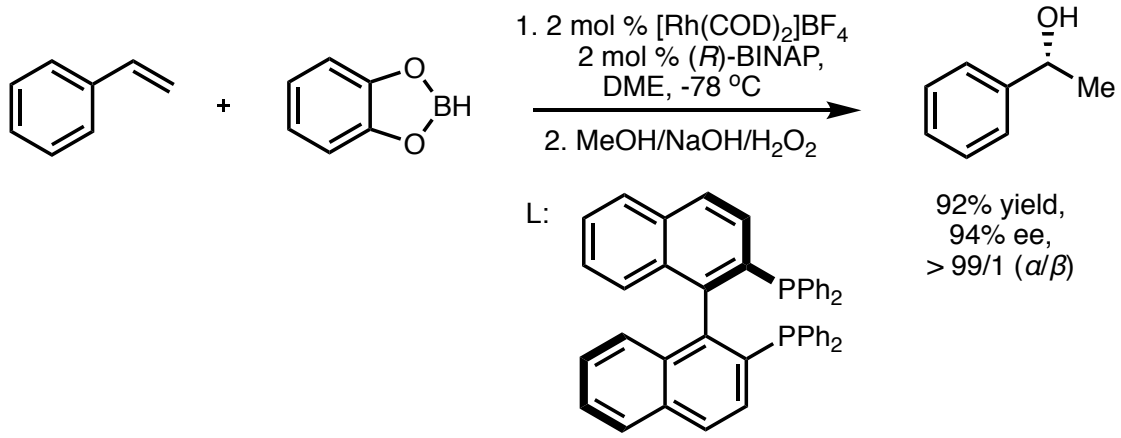
[2] Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449-16451.

[3] Carroll, A.-M.; O'Sullivan, T. P.; Guiry, P. J. *Adv. Synth. Catal.* **2005**, *347*, 609-631.

[4] Brown, H. C.; Subba Rao, B. C. *J. Am. Chem. Soc.* **1956**, *78*, 2582-2588.

[5] (a) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev*. **1991**, *91*, 1179-1191. (b) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695-4712.

Scheme 2.1 Regio- and Enantioselective Hydroboration of Alkenes Promoted by Rhodium-Based Catalyst



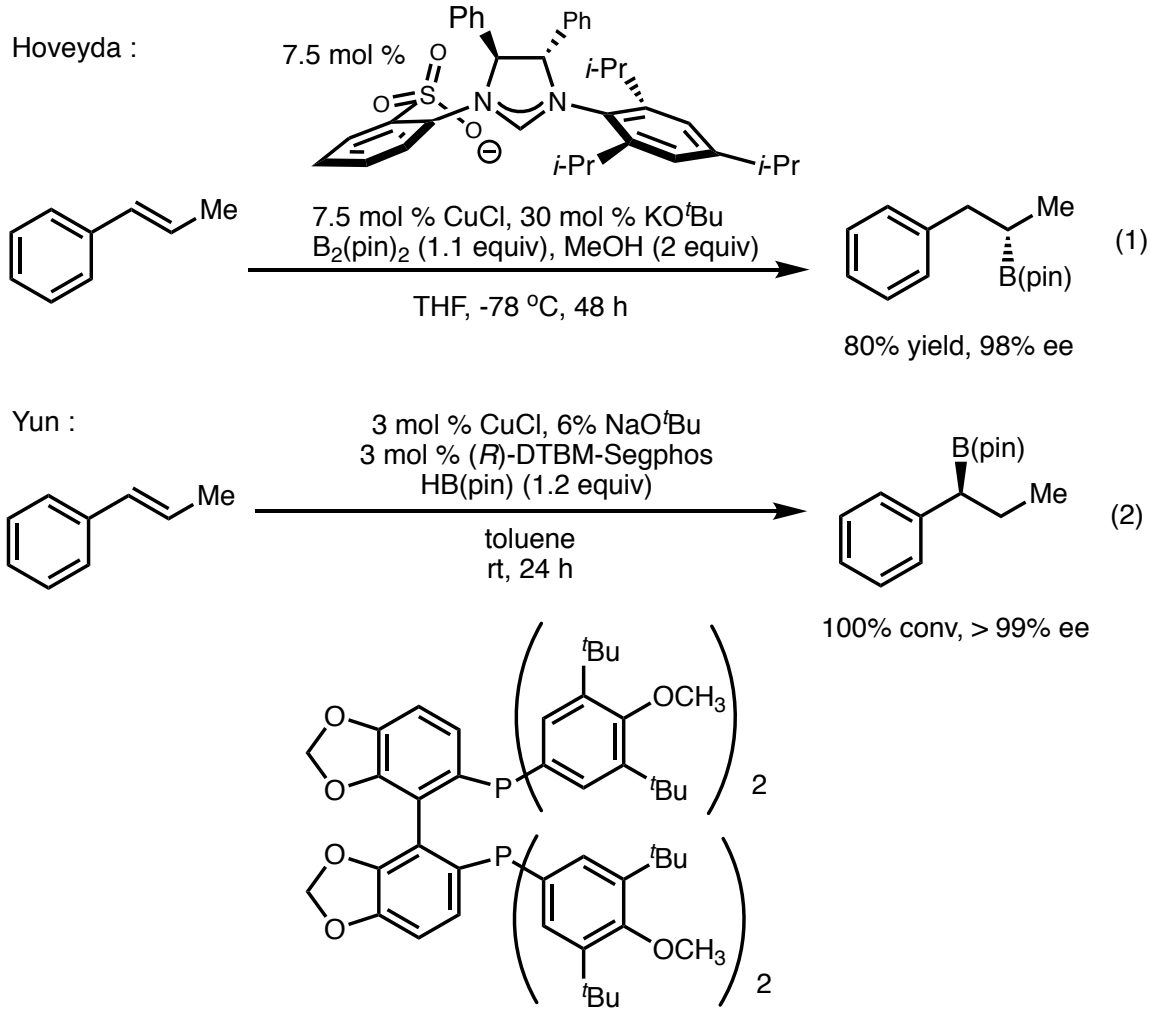
As mentioned above, one powerful method of constructing alkylboronic esters is hydroboration of alkenes. In 2009, Hoveyda[6] and Yun[7] independently reported that chiral copper-based complexes could catalyze enantioselective hydroboration of styrene derivatives to afford nonracemic benzylic boronic esters (Scheme 2.2). These two different systems delivered different regioisomeric products and were complementary to each other. In addition, Yun and coworkers disclosed a phosphine-Cu-catalyzed protocol for enantioselective β-boration of esters, amides and nitriles.

---

[6] Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160-3161.

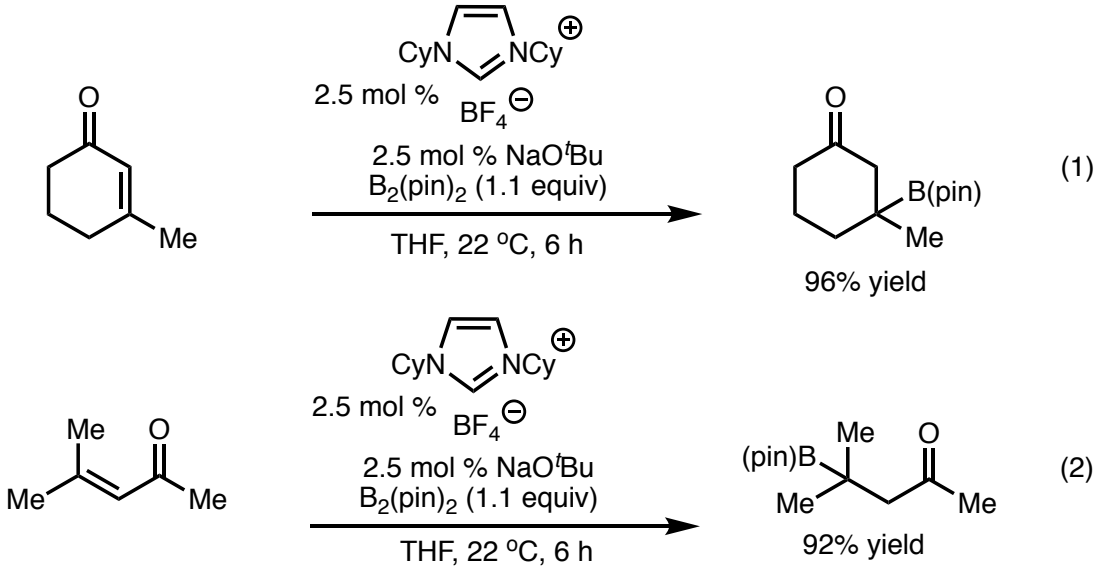
[7] Noh, D.; Chea, H.; Ju, J.; Yun, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6062-6064.

Scheme 2.2 Enantioselective Hydroboration of Alkenes Catalyzed by Chiral Copper-Based Complexes



In 2009, Hoveyda and coworkers reported the first transition metal-free *β*-boration of cyclic and acyclic *α*, *β*-unsaturated ketones[8] to construct tertiary and quaternary boronic esters efficiently (Scheme 2.3) with catalytic amounts of *N*-heterocyclic carbene (NHC) ligand. Five-, six-, seven-, and eight-membered- ring enones were all suitable substrates, affording *β*-boryl carbonyls with tertiary B-substituted carbons in good yield. Of note, this NHC-catalyzed process has better functional group tolerance than the Cu-catalyzed variant.

Scheme 2.3 First Metal-Free Borylation of Cyclic and Acyclic *α*,*β*-Unsaturated Ketones



[8] Lee, K. S.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7253-7255.

In 2007, Aggarwal and coworkers developed a stereospecific 1,2-metallate rearrangement[9] to assemble alkylboronates in a highly enantioselective fashion by using Hoppe-type lithiated carbamates (Scheme 2.4).[10] This is a highly effective method of making these compounds, however, a limitation of this methodology is the reliance of stoichiometric amounts of chiral sparteine that is not readily available. More recently, Marder and Liu developed a transition metal-catalyzed Miyaura-type boration[11] between primary, secondary and tertiary alkyl electrophiles with $B_2(pin)_2$ to furnish mono boronic esters (Scheme 2.5).

In this chapter, I will present a new strategy to make alkylboronic esters.

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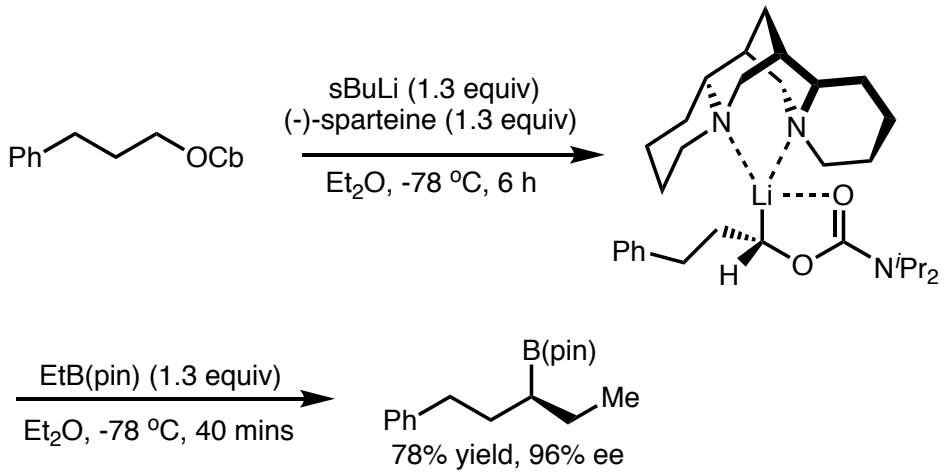
[9] Stymiest, J. L.; Dutheuil, G.; Mahmood, A.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2007**, *46*, 7491-7494.

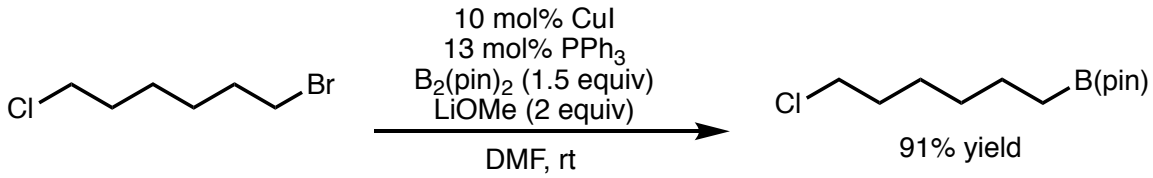
[10] Hoppe, D.; Hintze, F.; Tebben, P.; Paetow, M.; Ahrens, H.; Schwerdtfeger, J.; Sommerfeld, P.; Haller, J.; Guarnieri, W.; Kolczewksi, S.; Hense, T.; Hoppe, D. *Pure Appl. Chem.* **1994**, *66*, 1479-1486.

[11] Yang, C.-T.; Zhang, Z.-Q.; Tajuddin, H.; Wu, C.-C.; Liang, J.; Liu, J.-H.; Fu, Y.; Czyzewska, M.; Steel, P. G.; Marder, T. B.; Liu, L. *Angew. Chem., Int. Ed.* **2012**, *51*, 528-532.

Scheme 2.4 Lithiation and Borylation of Hoppe-type Carbamates



Scheme 2.5 Copper Catalyzed Borylation of Alkyl Halides



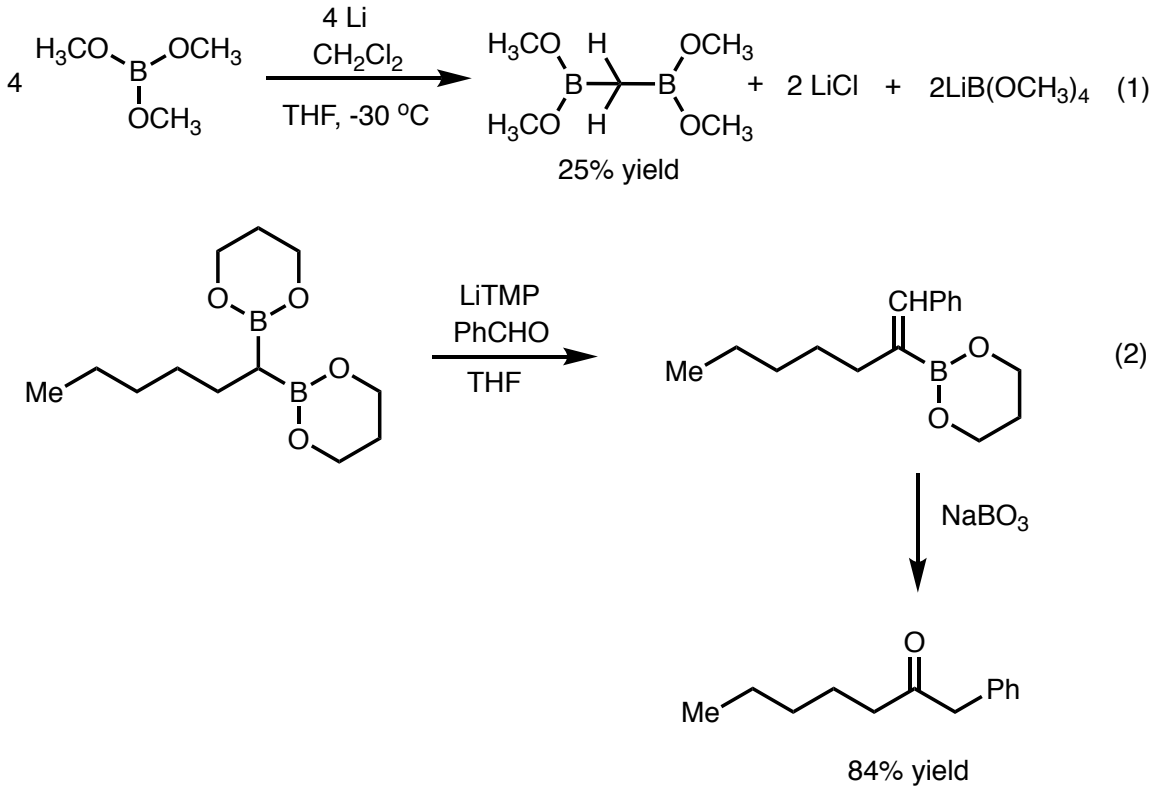
2.2 Background

Matteson and co-workers accomplished the synthesis of a variety of geminal bis(boronic) esters[12] from trimethyl borate, dichloromethane and lithium reagents (Scheme 2.6, Equation 1). The obtained germinal bis(boronates) were then allowed to

[12] Castle, R. B.; Matteson, D. S. *J. Organomet. Chem.* **1969**, *20*, 19-28.

react with aldehydes, followed by oxidation to deliver carbonyl compounds[13] (Scheme 2.6, Equation 2). However, this strategy to access 1,1-dibory alkanes was neither convenient nor safe to operate; also, functional group compatibility was found to be limited.

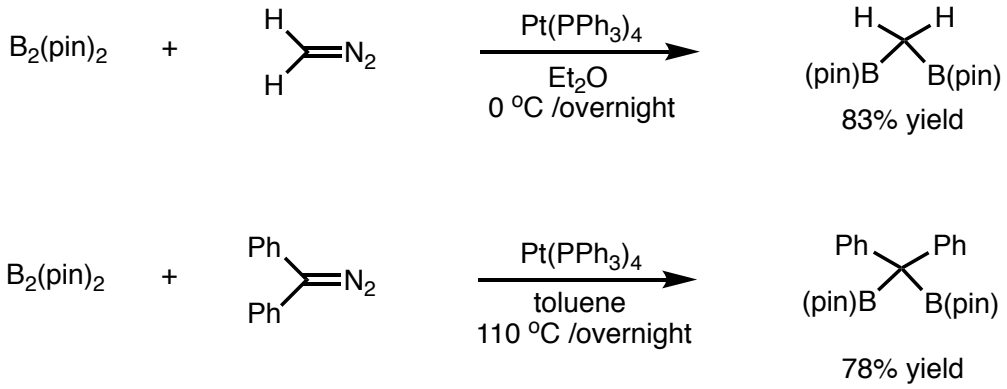
Scheme 2.6 Synthesis of Geminal Bis(Boronates) and Further Transformations



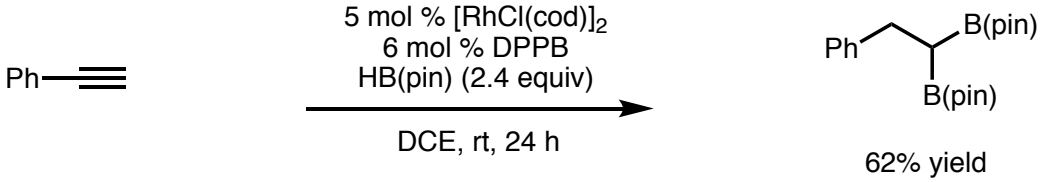
[13] Matteson, D. S.; Moody, R. J. *Organometallics*, **1982**, *1*, 20-28.

In 2002, Srebnik and coworkers[14] reported that bis(pinacolato)diborane could insert into diazoalkanes with a platinum-based catalyst to afford 1,1-diboryl compounds (Scheme 2.7). In 2009, Shibata *et al*[15] revealed that Rh(I)Cl–DPPB-complex could promote consecutive hydroboration of alkynes to furnish 1,1-bis(boronic) esters (Scheme 2.8). However, both methods suffered from limited substrate scope. Utility of 1,1-bis(boronic) esters in organic synthesis was probably hampered due to the associated difficulties in their preparation during that time.

Scheme 2.7 Synthesis of Geminal Bis(Boronates) From Diazo Compounds



Scheme 2.8 Synthesis of Geminal Bis(Boronates) From Alkynes



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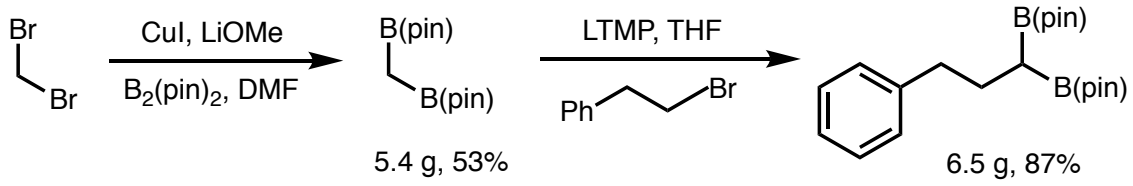
[14] (a) Abu Ali, H.; Goldberg, I.; Srebnik, M. *Organometallics* **2001**, *20*, 3962-3965. (b) Abu Ali, H.; Goldberg, I.; Kaufmann, D.; Burmeister, C.; Srebnik, M. *Organometallics* **2002**, *21*, 1870-1876.

[15] Endo, K.; Hirokami, M.; Shibata, T. *Synlett* **2009**,1331-1335.

In 2014, our group reported that 1,1-dibromoalkanes can be converted to geminal bis(boronates) using copper iodide as the catalyst. Following that, we were able to scale up this transformation to obtain 1,1-diborylmethane. Following the precedence established by Matteson,[16] the generated 1,1-bis(boronates) could be deprotonated by lithium tetramethylpiperidide (LiTMP) and subsequently alkylated with electrophiles to furnish a diverse range of substituted 1,1-diborylalkanes (Scheme 2.9). These geminal bis(boronates) were then subjected to deborylative alkylation reaction to deliver mono-substituted boronic ester products. At the same time, Marder and Fu developed similar Cu-catalyzed methods to obtain 1,1-diborylalkanes.[17]

Scheme 2.9 Synthesis of Geminal Bis(Boronates) On Gram Scale

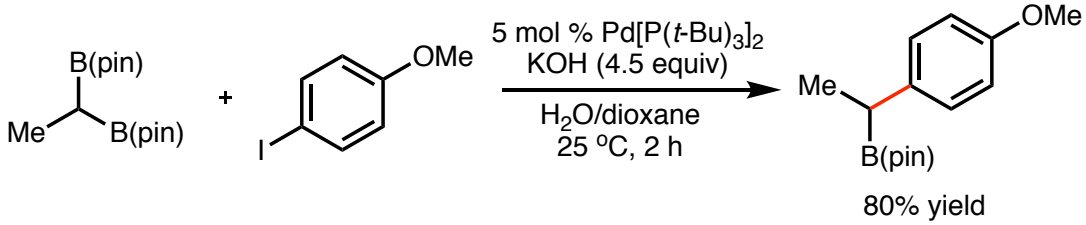


[16] Matteson, D. S.; Moody, R. J. *Organometallics*, **1982**, *1*, 20-28.

[17] Zhang, Z.-Q.; Yang, C.-T.; Liang, L.- J.; Xiao, B.; Lu, X.; Liu, J.-H.; Marder, T. B.; Fu, Y. *Org. Lett.* **2014**, *16*, 6342-6345.

1,1-Bis(boronic) esters[18] constitute a valuable class of compounds because of their unique reactivity. In 2010, Shibata and coworkers[19] reported that alkyl geminal bis(boronates) can undergo Suzuki coupling with aryl halides to afford secondary boronic esters (Scheme 2.10). It was reasoned that after rapid transmetallation, the empty p orbital of boron could help to stabilize the σ-alkylpalladium intermediate, thus reducing the propensity of *β*-H elimination.

Scheme 2.10 First Suzuki Coupling Between Alkyl Geminal Bis(Boronates) and Aryl Halides



In 2014, Morken and coworkers[20] developed an enantioselective variant of this Suzuki coupling between geminal bis(boronates) and aryl halides in the presence of $Pd(OAc)_2$ and a taddol-derived phosphoramidite ligand (Scheme 2.11). A broad scope of

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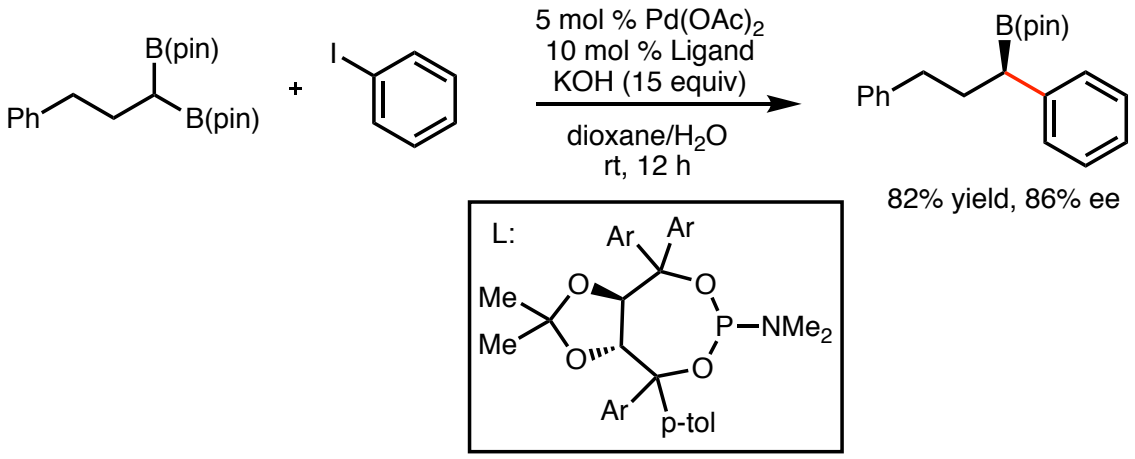
[18] Hall, D. G. *Boronic Acids*, 2nd ed.; Wiley-VCH: Weinheim, **2011**.

[19] Endo, K.; Ohkubo, T.; Hirokami, M.; Shibata, T. *J. Am. Chem. Soc.* **2010**, *132*, 11033-11035.

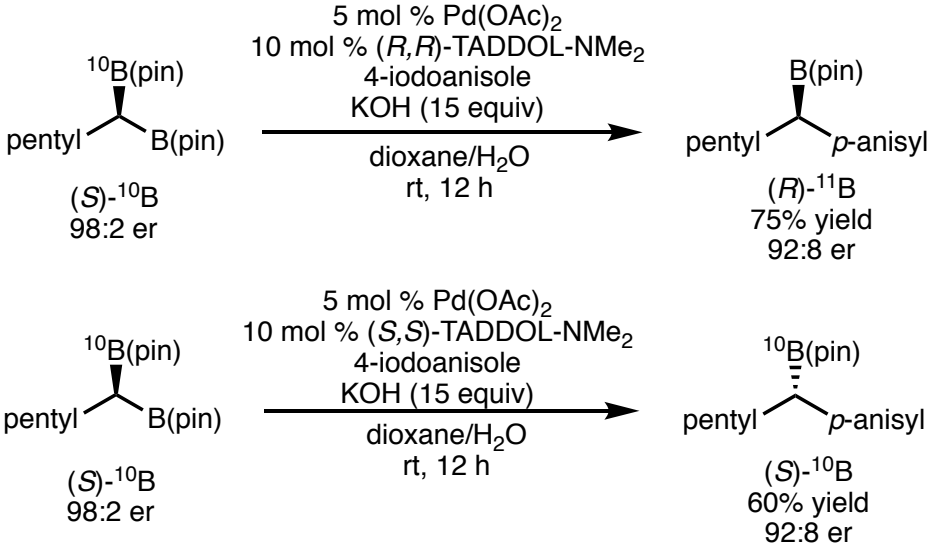
[20] Sun, C.; Porter, B.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 6534-6537.

substrates ranging from electron-donating to slightly electron-withdrawing aryl halides could be employed. Studies were also carried out to gain mechanistic insights (Scheme 2.12). Enantioenriched ^{10}boron-labeled 1,1-diboryl alkanes were subjected to the reaction conditions, and the mono-substituted boronic ester products were then collected and analyzed by mass spectrometry. From the obtained data, it was concluded that transmetallation from the putative boron ate complex to palladium occurred in a stereoinvertive fashion.

Scheme 2.11 First Enantioselective Suzuki Cross Coupling between Geminal Bis(Boronates) and Aryl Halides



Scheme 2.12 Mechanistic Studies Revealed the Carbon Center Inverted Transmetallation



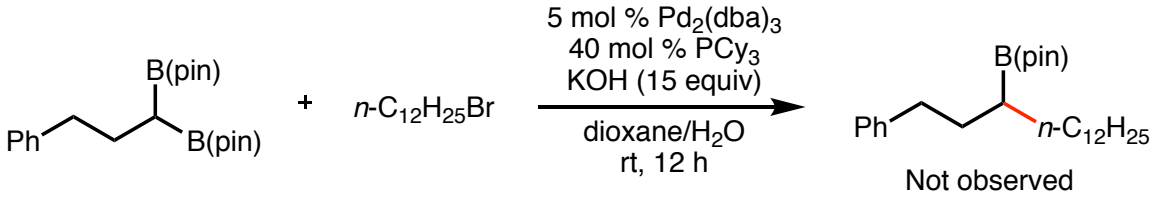
Our efforts focused on expanding the scope of the aforementioned Suzuki coupling from aryl halides to alkyl halides. We envisioned that such transformations that merge 1,1-diboryl alkanes with alkyl electrophiles enantioselectively could have a profound impact in synthetic chemistry. We anticipated that β-H elimination is a likely competitive side pathway that needs to be circumvented for the success of our proposed method.

2.3 Development of Deborylative Alkylation Reaction

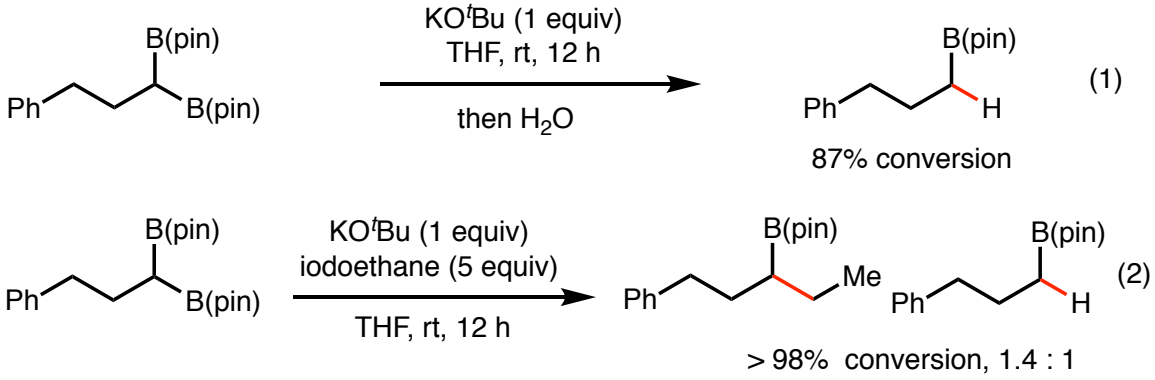
2.3.1 Preliminary Studies Involving Pd-Catalyzed Suzuki Coupling Between Alkyl Bis(boronates) and Alkyl Halides

On the basis of our earlier studies, Suzuki coupling reactions between alkyl geminal bis(boronic) esters and 1-bromododecane were initially examined (Scheme 2.13) using monodentate ligands such as PCy_3 and Ruphos. However, none of the desired cross coupling products were detected in any attempts. We then proceeded to probe the background reaction in the presence of base, but without the Pd-based catalyst (Scheme 2.14, equation 1). This experiment revealed only the presence of protodeborylation product.

Scheme 2.13 Attempt Enantioselective Suzuki Coupling Between Alkyl Geminal Bis(Boronates) and Alkyl Halides



Scheme 2.14 Background Reaction of Suzuki Coupling Between Alkyl Geminal Bis(Boronates) and Alkyl Halides



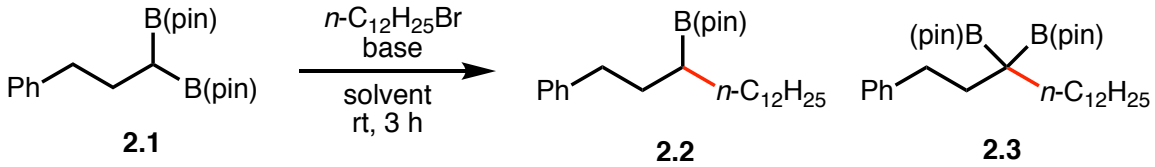
To learn about the capacity for protodeborylation under anhydrous conditions, and the potential for cross-coupling in the absence of water, we examined background reaction in the THF solvent. As demonstrated in Scheme 2.14, we observed significant amount of protodeborylation byproduct when the background reaction was performed overnight and quenched with wet diethyl ether. At this point, we wondered if other electrophiles such as alky halides could be utilized as an electrophile in place of water to forge a carbon-carbon bond instead of carbon-hydrogen bond. To test this, the aforementioned reaction was repeated in the presence of excess iodoethane (Scheme 2.14, equation 2). Full consumption of starting material and 58% conversion to the desired deborylative alkylated product was observed. While our initial attempts to achieve enantioselective Suzuki coupling appeared fraught with complication, the base-promoted

deborylative alkylation reaction[21] as a tool to construct primary, secondary, and tertiary alkyl boronic esters for synthetic chemistry was then developed.

2.3.2 Reaction Optimization

With preliminary results in hand, we tested different bases and solvents in order to find the optimal reaction conditions (Table 2.1). Potassium hydroxide, the requisite base for enantioselective Suzuki cross coupling between geminal bis(boronates) and aryl halides, was discovered to be inefficient in our system. Among LiO^tBu, NaO^tBu and KO^tBu, we found out that NaO^tBu served as the optimal base, as it possesses the best balance of base strength to ensure good reactivity without promoting adventitious side reactions (such as elimination of the alkyl halides). Experiments also showed that reactions performed in polar solvents were generally more efficient (vs. non-polar solvents), which led us to conclude that NaO^tBu in THF were the best reaction conditions for the deborylative alkylation.

Table 2.1 Full Optimization Table



2.1 **2.2** **2.3**

[21] Hong, K.; Liu, X.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 10581-10584.

entry	base	solvent	conversion (%)	yield of 2.2 (%)
1	KOH	THF	<5	-[b]
2	LiO^{t}Bu	THF	<5	-[b]
3	NaO^{i}Pr	THF	<5	-[b]
4	NaO^{t}Bu	THF	100	91
5	NaO^{t}Amyl	THF	85	72
6	NaN(SiMe$_3$)$_2$	THF	100[d]	-
7	KOMe	THF	30	-
8	KO^{t}Bu	THF	100	68
9	NaO^{t}Bu	THF	65	46[c]
10	NaO^{t}Bu	dioxane	75	70
11	NaO^{t}Bu	ether	<5	-[b]
12	NaO^{t}Bu	CH_2Cl_2	<5	-[b]
13	NaO^{t}Bu	hexanes	<5	-[b]
14	NaO^{t}Bu	toluene	<5	-[b]
15	KO^{t}Bu	toluene	80	76
16	NaO^{t}Bu	THF	100	97[e]
17	NaO^{t}Bu	THF	67	-[f, g]
18	KO^{t}Bu	toluene	100	97[f, h]

[a] Reaction conditions: 1-bromododecane (0.10 mmol, 0.2 M), **2.1** (0.13 mmol) and base (0.30 mmol). Conversion refers to consumption of 1-bromododecane and was determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as the internal standard. Yield refers to the isolated yield of purified material. [b] partial protodeboronation of **2.1**. [c] 1.5 equiv. NaO^{t}Bu employed instead of 3.0 equiv. [d] exclusively **2.3**. [e] 14 hours. [f] 1-chlorododecane employed instead of 1-bromododecane. [g] **2.2**:**double alkylation product** = 2.5:1. [h] 2.0 equiv. **2.1**, 5.0 equiv. KO*t*-Bu, toluene, 14 hours.

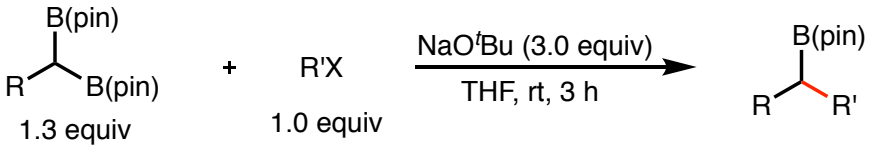
2.3.3 Substrate Scope

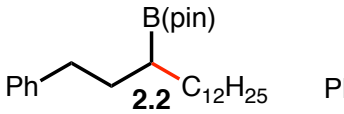
With the established conditions in hand, we proceeded to assess the generality of the protocol with a wide array of electrophiles (Scheme 2.14). Alkyl chlorides, bromides and iodides were effective substrates for this transformation, delivering desired product

2.2 in good yields. Alkyl iodides gave lower yields of **2.2** due to competitive elimination side reactions. Secondary alkyl halides could also be employed to give **2.4** in 75% yield. For substrates bearing both primary and secondary alkyl halides, reaction occurred chemoselectively at the primary position (**2.5)**. Not surprisingly, allylic halides (**2.6**, **2.7**, **2.8** and **2.9**) and benzylic halides (**2.11** and **2.12**) afforded deborylative alkylated products efficiently in 74–91% yield. Non-substituted 1,1-diborylalkanes can similarly undergo reaction to furnish primary boronic ester products (**2.10**, **2.11** and **2.12**), and sterically hindered geminal bis(boronate) ester was efficiently converted to desired product **2.13** in 87% yield.

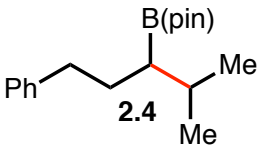
The substrate scope for deborylative alkylation reaction was extended from terminal bis(boronates) to more sterically congested internal geminal bis(boronic) esters (Scheme 2.15). To our surprise, the steric hindrance did not jeopardize reactivity, as the alkylated product (**2.14**) could be isolated in 95% yield. The tethered alkene (**2.16**) and cyclopropyl group (**2.18**) were found to be intact under the reaction conditions, suggesting that radical intermediates are unlikely to be generated during the course of the reaction. Geminal bis(boryl) cyclopropanes were also effective substrates in this protocol, delivering alkylated products in good yields and high diastereoselectivities (**2.17** and **2.19**).

Scheme 2.14 Substrate Scope for Building Primary and Secondary Boronic Esters

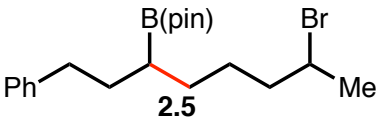




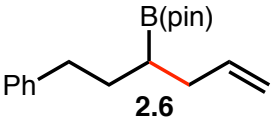
X = Br 91%(gram scale)
X = Cl 97%
X = I 76%



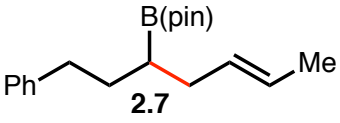
X = Br, 75%



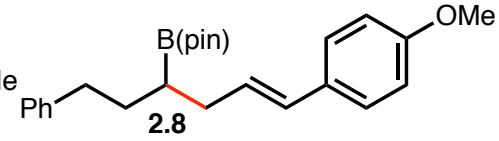
X = Cl, 84%



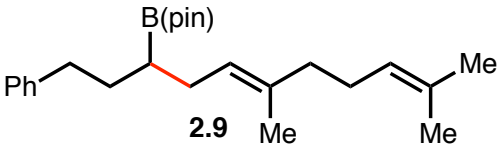
X = Cl, 86%



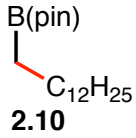
X = Cl, 91%



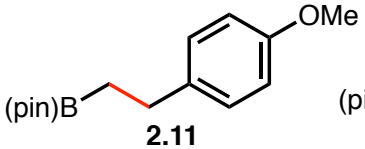
X = Cl, 78%



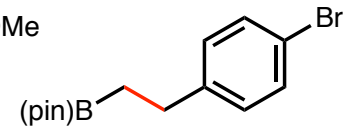
X = Cl, 90%



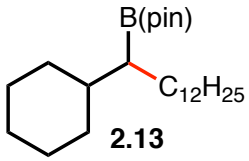
X = Cl, 90%



X = Cl, 74%

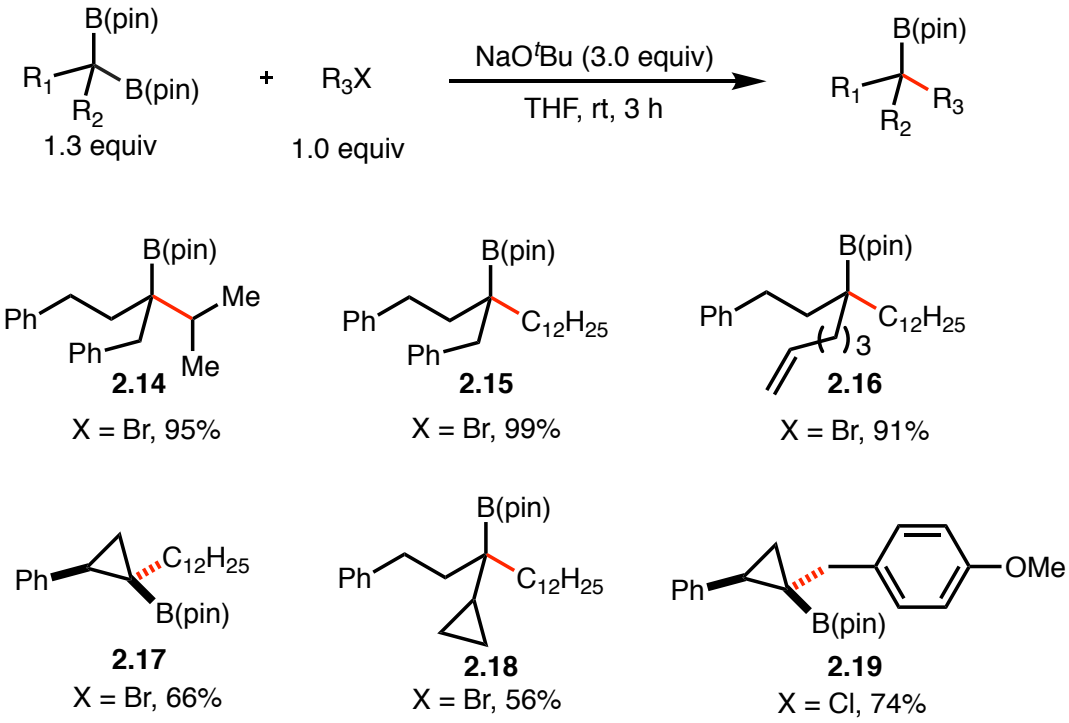


X = Cl, 77%



X = Br, 87%

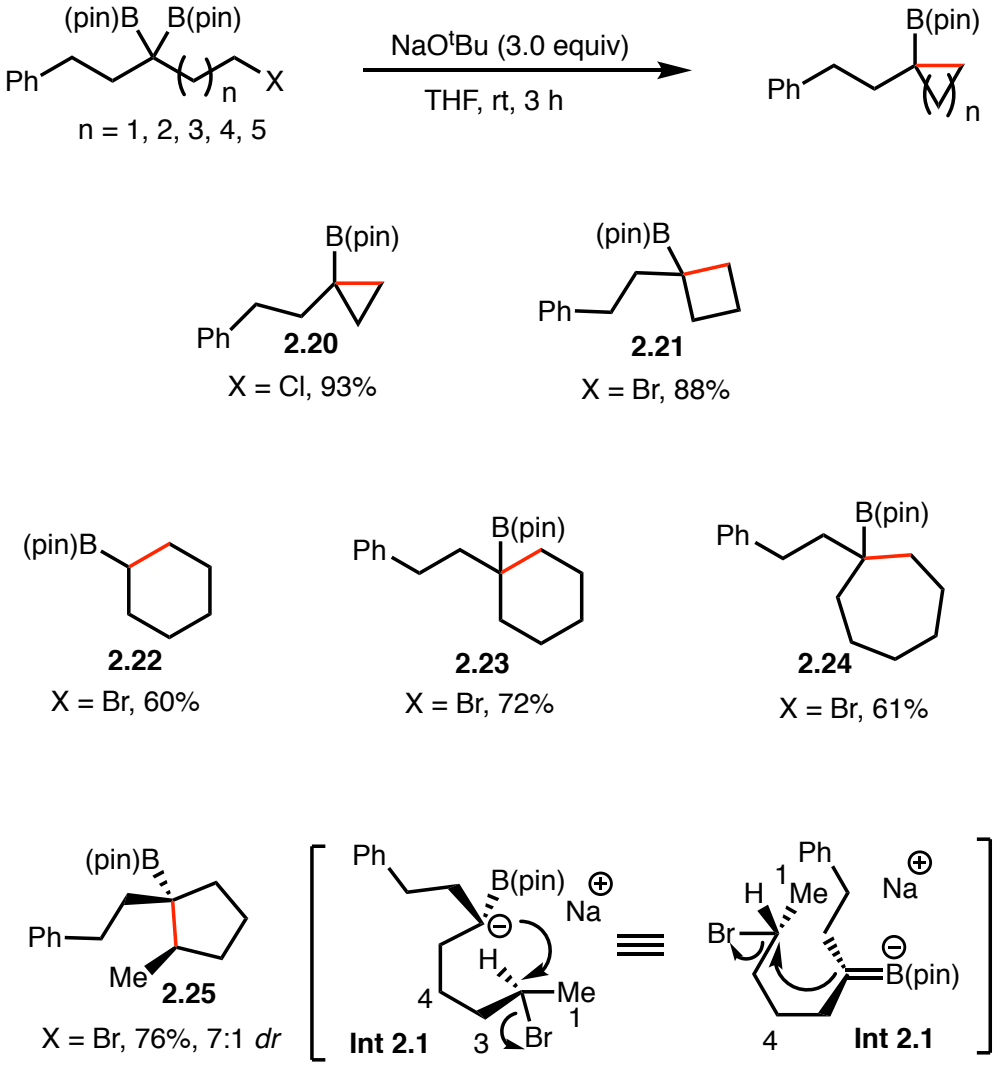
Scheme 2.15 Substrate Scope for Constructing Tertiary Boronic Esters



Intramolecular variants of the deborylative alkylation reaction to afford carbocyclic boronic esters could also be accomplished. As demonstrated below (Scheme 2.16), products ranging from three-membered to seven-membered ring systems could be prepared, although yields appeared to diminish with the size of the carbocycles. This could be due to the increased conformational flexibility in substrates bearing longer alkyl chains, rendering undesired intermolecular reactions to be competitive with intramolecular cyclization. Of note, the secondary bromide substrate afforded the

cyclopentane ring **2.25** in high diastereoselectivity. The steric interaction between methyl group at C1 and C4 shown in **Int 2.1** might be the origin of the diastereoselectivity, also, the proton would prefer the spot near sterically congested boronic ester.

Scheme 2.16 Substrate Scope for Intramolecular Deborylative Alkylation Reactions



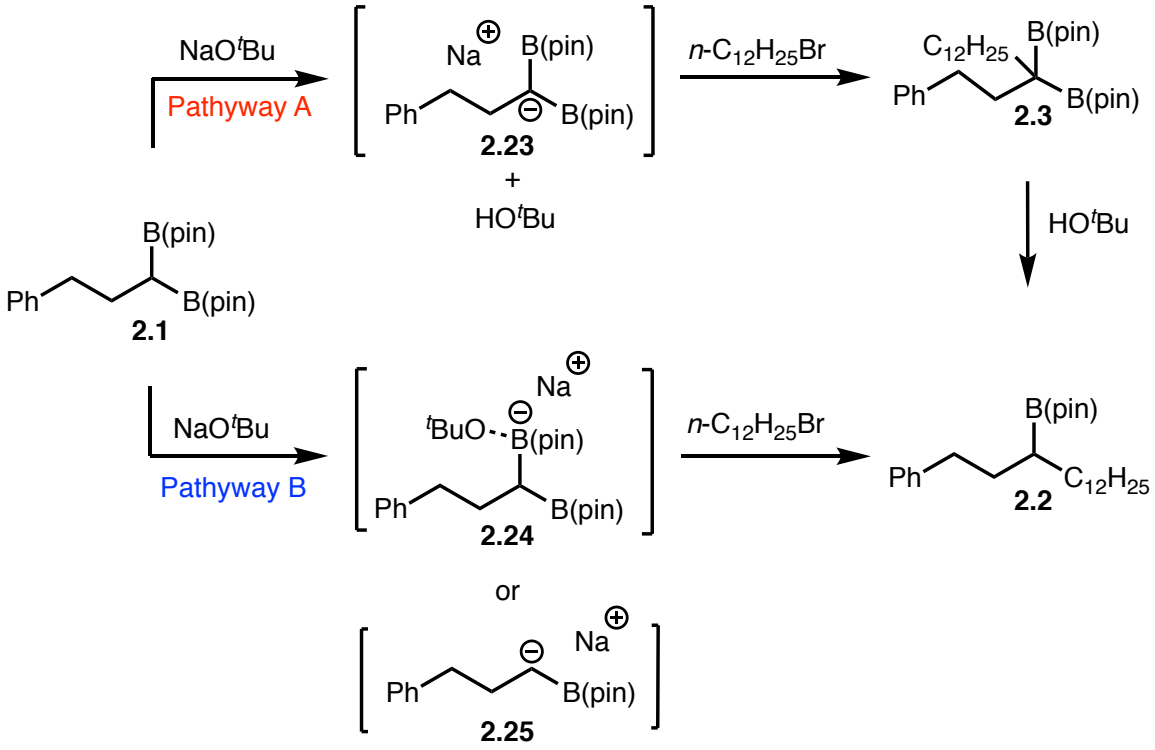
2.3.4 Mechanistic Studies

Based on the aforementioned observations, we proposed two possible mechanistic pathways for this transformation (Scheme 2.18). The first possible pathway involves deprotonation of geminal bis(boronic) ester **2.1** with NaO^{t}Bu to generate carbanion species **2.23** and *tert*-butanol. **2.23** may then react with 1-bromododecane to afford geminal bis(boronic) ester **2.3**, which subsequently undergoes protodeborylation with *tert*-butanol to deliver desired product **2.2**. Alternatively, NaO^{t}Bu may first react with one of the B(pin) (pin: pinacolato) units through coordination to furnish either boron ate complex **2.24** or a-boryl carbanion **2.25** before reacting with 1-bromododecane to give **2.2**.

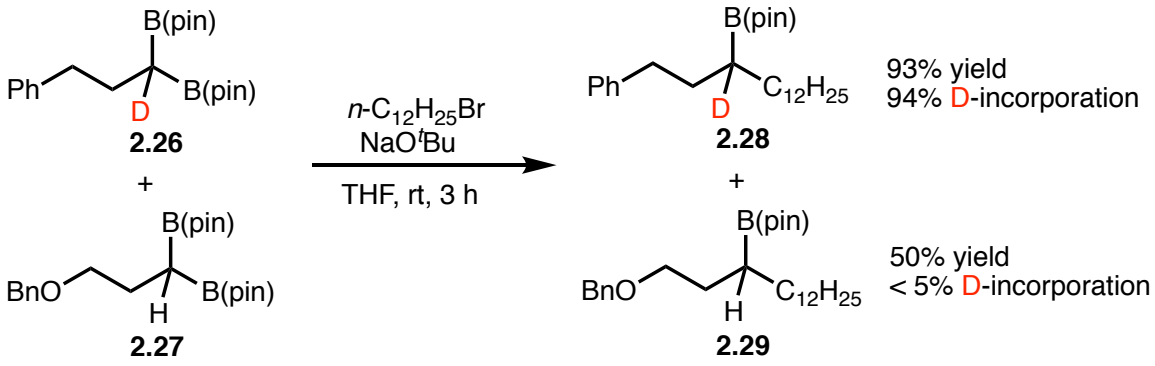
To distinguish between these two pathways (Scheme 2.19), we prepared deuterium-labeled substrate **2.26** and non-deuterated 1,1-bisborylalkane **2.27**. These two compounds were subjected to the established reaction conditions in the same flask. If Pathway A was to be operative, the generated deuterium-labeled *tert*-butanol could react with both substrates through deuterium-boron exchange to furnish two products with significant amounts of deuterium incorporation. If pathway B was the dominant process, no deuterium scrambling shall be expected. In the event, the crossover experiment revealed minimal loss of deuterium content within product **2.28** and <5% deuterium

incorporation in product **2.29**. These results were indicative of Pathway B being the most likely mechanism through which the deborylative alkylation proceeds.

Scheme 2.18 Two Possible Pathways for Deborylative Alkylation Reaction

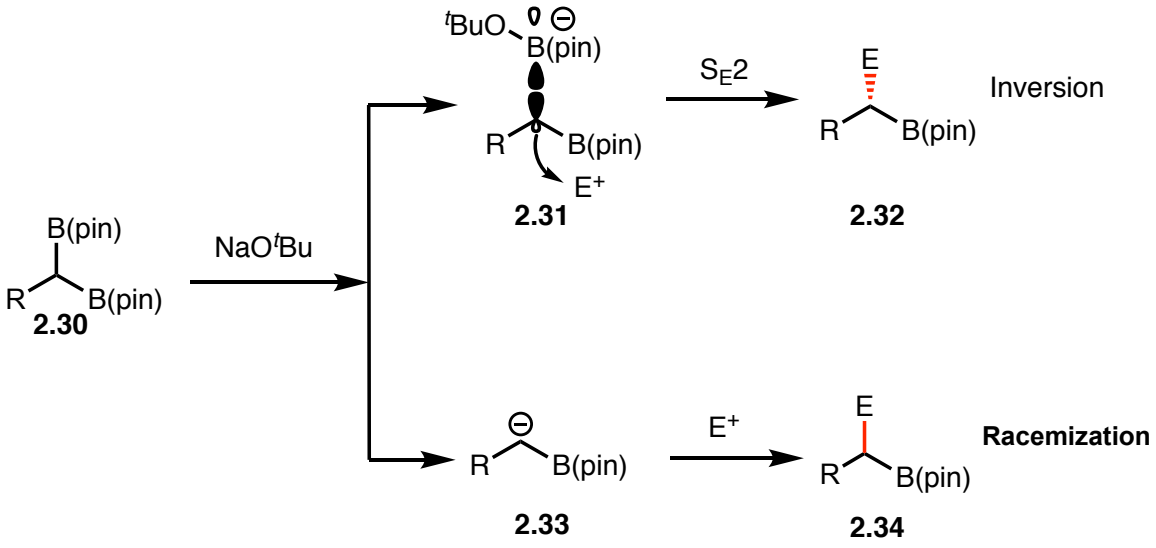


Scheme 2.19 Crossover Experiment to Differentiate Pathway A and Pathway B



Question that remains is whether the transformation proceeds through the intermediacy of boron ate complex **2.24** or carbanion **2.25**. Based on literature precedence, we found that borate complexes usually react with electrophiles through a S_E2 inverted manner,[22] while a carbanion would give rise to racemic product (Scheme 2.20).

Scheme 2.20 Different Mechanisms Leading to Different Stereochemical Outcomes



To distinguish between these two possibilities, we synthesized ^{10}B-labeled enantioenriched 1,1-diborylalkane **2.39** (Scheme 2.21). Starting from commercial

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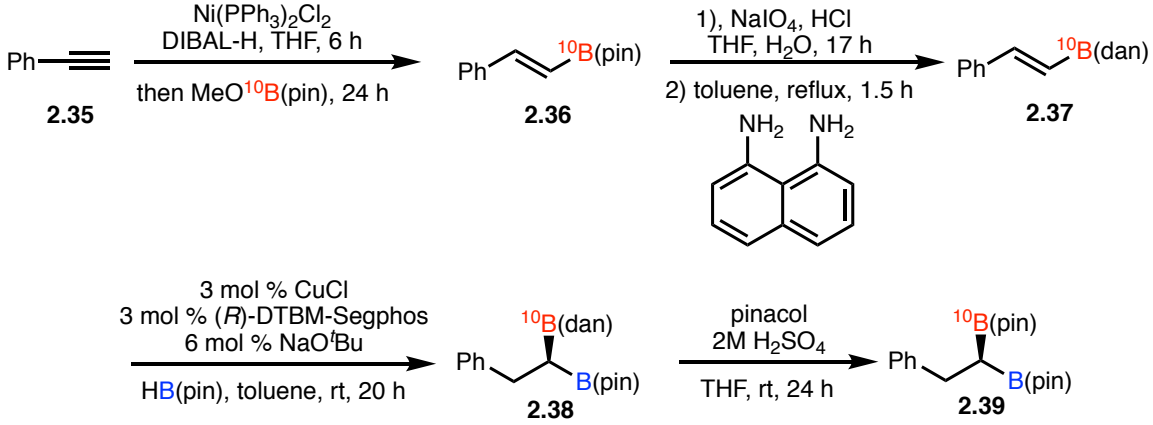
[22] Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2011**, *133*, 16794-16797.

available phenylacetylene **2.35**, nickel-catalyzed regioselective hydroalumination [23] followed by trapping with ^{10}B-labeled MeO^{10}B(pin) furnished *E*-alkenyl-^{10}B(pin) **2.36**. The B(pin) motif was oxidatively cleaved and the resulting boronic acid was refluxed with 1,8-diaminonaphthalene to give *E*-alkenyl-^{10}B(dan) **2.37**. Copper-catalyzed enantioselective hydroboration[24] with styrene derivative **2.37** gave 1,1-bisborylalkane **2.38**, which was then converted to the desired ^{10}B-labeled geminal bis(boronic) ester **2.39**.

Scheme 2.21 Synthesis of ^{10}B-Labeled Enantioenriched Geminal Bis(boronate) Ester **2.39**

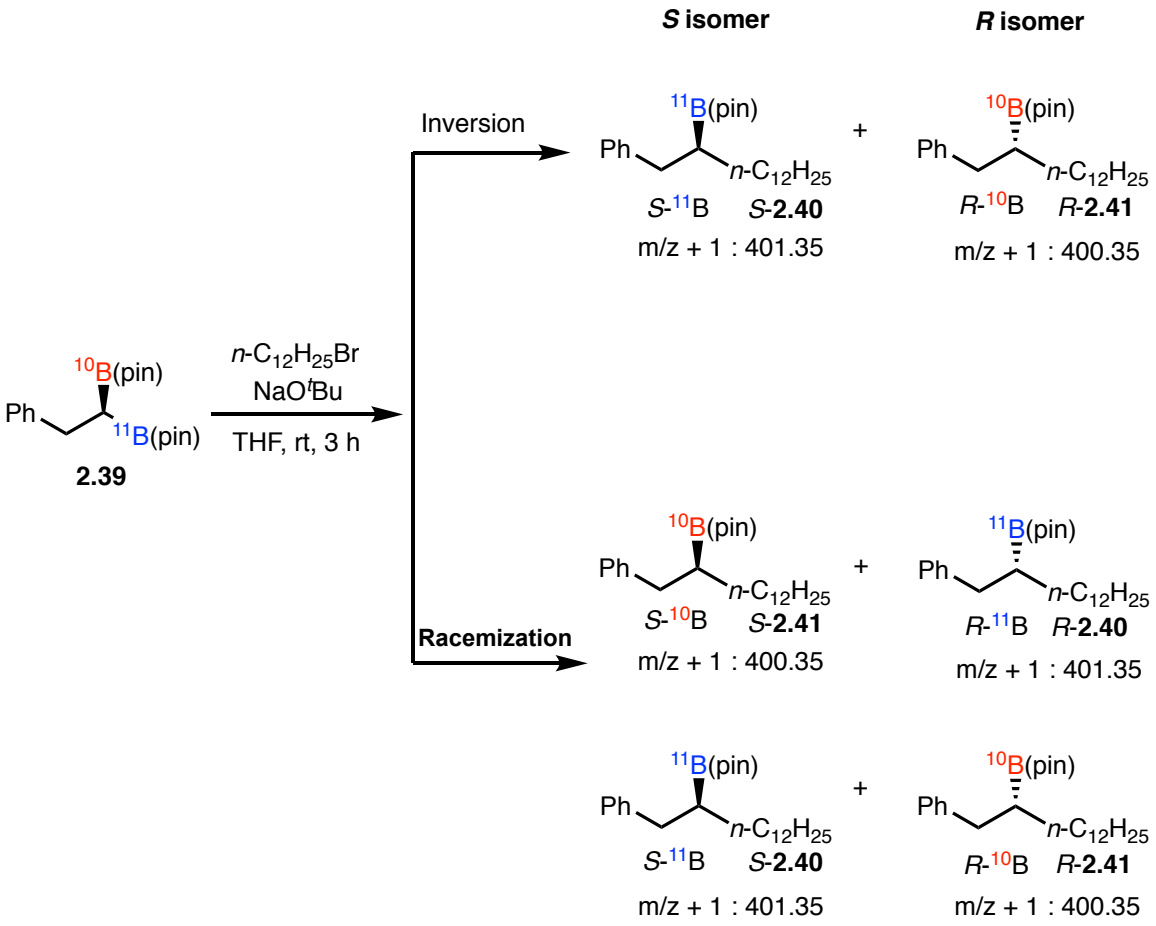


[23] Gao, F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10961-10963.

[24] Feng, X.; Jeon, H.; Yun, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 3989-3992.

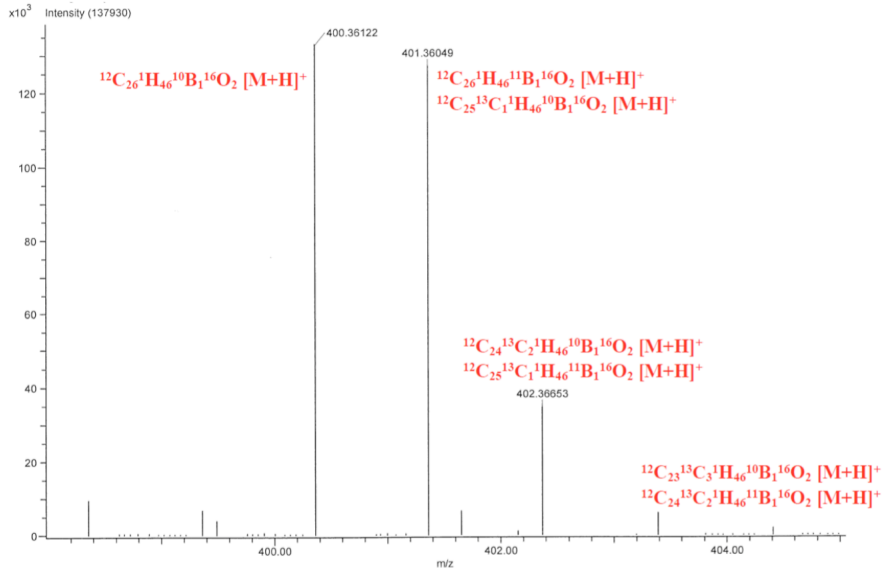
Enantioenriched 1,1-diborylalkane **2.39** was treated with NaO^{t}Bu and 1-bromododecane. After silica gel column chromatography, the obtained products were separated by supercritical fluid chromatography (SFC), and the isolated (*S*)- and (*R*)-enantiomers were then analyzed by mass spectrometry. The hypothesis is that if deborylative alkylation occurs through stereoinvertive electrophilic substitution, the mass balance for the two enantiomers (*S*)-**2.40** and (*R*)-**2.41** should be different. On the other hand, the isotopic composition for both enantiomers should be identical if racemization does happen. (For (*S*)-enantiomer, there would be ^{10}B-**2.41** and ^{11}B-**2.40**; for (*R*)-enantiomer, there would be ^{10}B-**2.41** and ^{11}B-**2.40**).

Scheme 2.22 Calculated Results for Possible Pathways

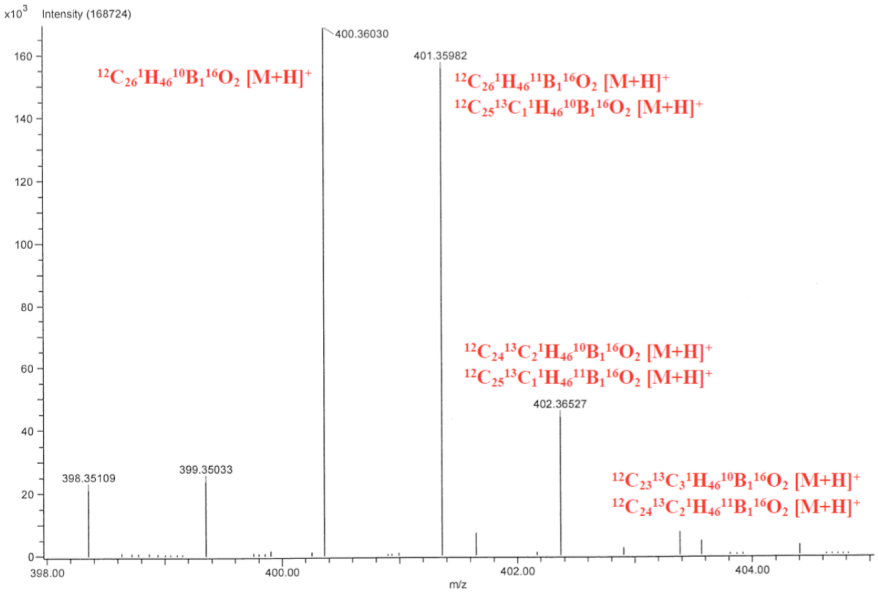


The two almost identical mass spectra (Scheme 2.23 and Scheme 2.24) obtained for (*S*)-enantiomer and (*R*)-enantiomer led us to conclude that the carbon stereocenter was racemized during the reaction process, implying that carbanion **2.33** was most likely generated as the reactive intermediate.

Scheme 2.23 Mass Spectrum of Product (*S*) Enantiomer from ^{10}B-labeled Experiment Using (*S*)-^{10}B-**2.39**:



Scheme 2.24 Mass Spectrum of Product (*R*) Enantiomer from ^{10}B-labeled Experiment Using (*S*)-^{10}B-**2.39**:



To further support our hypothesis for the existence of carbanion **2.33**, we synthesized ^{13}C-labeled geminal bis(boronate) ester **2.42** and subjected it to NaO^{t}Bu and d_8-THF in an NMR tube in the glovebox. Reaction progress was monitored by ^{13}C NMR spectrometry (Scheme 2.25). After adding base for 30 minutes, two new signals appeared. The smaller resonance at 27.1 ppm was attributed to protodeborylation byproduct **2.43**, and the broad one at 35.5 ppm was assigned as the boron-ate complex **2.44**. After 90 minutes, a new broad signal emerged at 49.1 ppm, which was believed to be the carbanion species **2.45**. The chemical shift is significantly downfield compared to typical carbanions (-15.3 ppm for MeLi[25]), which may be rationalized by the double bond character of the carbon-boron bond in **2.46**. As reaction proceeds, the peak at 49.1 ppm grew in size. As soon as 1-bromododecane was added, the broad signal that corresponds to **2.45** disappeared immediately and a new large peak at 31.4 ppm (later found to be due to the desired product **2.47**) was observed. This ^{13}C NMR study clearly demonstrated that base-promoted deborylative alkylation proceeds through the intermediacy of boron-stabilized carbanion species.

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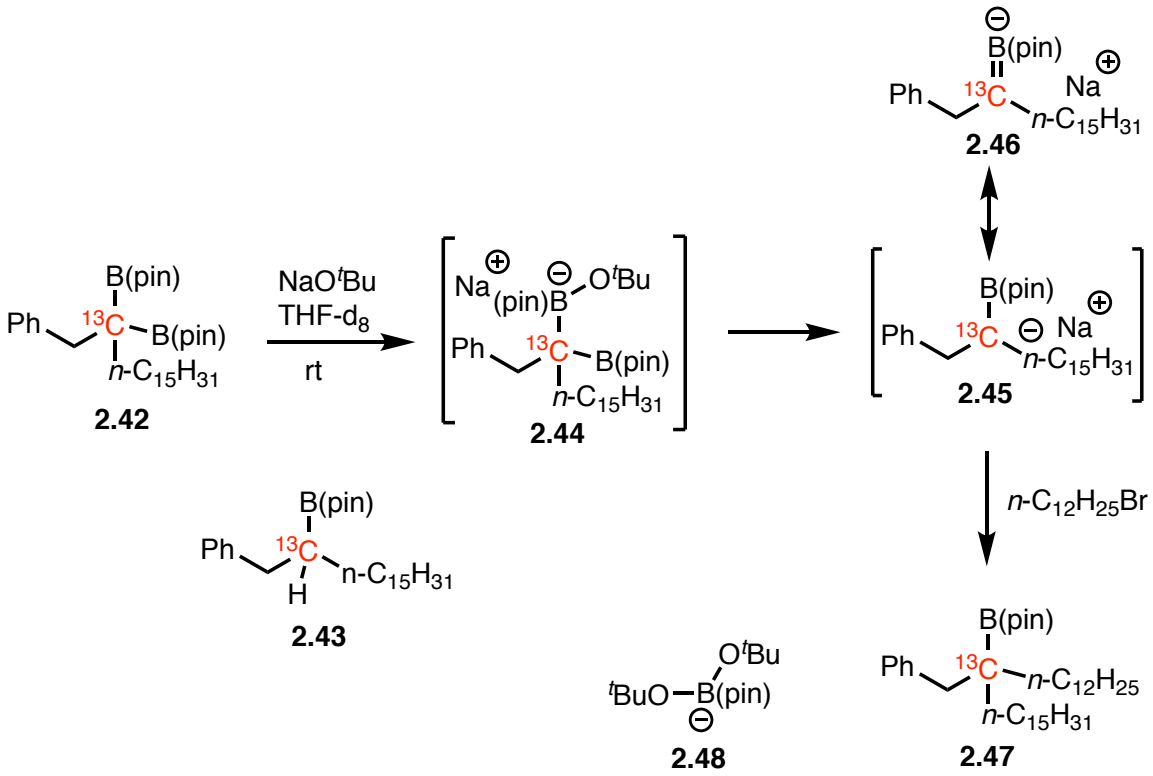
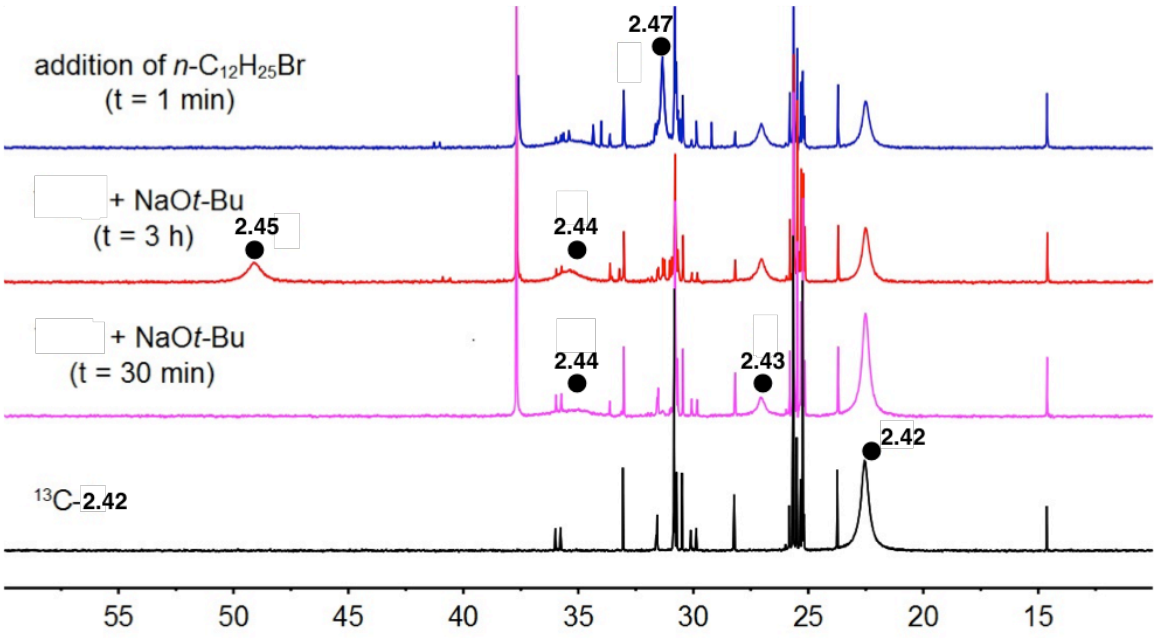
[25] Al-Humydi, A.; Garrison, J. C.; Youngs, W. J.; Collins, S. *Organometallics* **2005**, *24*, 193-196.

We also attempted to obtain evidence of the boron-stabilized carbanion intermediate *via* ^{11}B NMR spectrometry. However, the spectra were not very informative due to the presence of byproduct **2.48** occuring around 6 ppm. ^{13}Carbon-^{11}Boron correlation NMR spectra might be helpful in the further studies.

Scheme 2.25 ^{13}C NMR Study of ^{13}C-Labeled Geminal Bis(boronate) Ester **2.42**





2.4 Conclusions

The base-promoted deborylative alkylation reactions can afford synthetically useful primary, secondary and tertiary organoboronic esters from readily accessible 1,1-diboryl alkanes, and these products are amenable to further transformations to amines and alcohols in a stereoretentive fashion. Through extensive mechanistic studies, we found that these transformations proceed through the intermediacy of boron-stabilized carbanions.

2.5 Experimental Section

2.5.1 General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), or a Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm, THF-d_8: 3.58 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qi = quintet, sx = sextet, sp = septet, m = multiplet, br = broad), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.0 ppm, THF-d_8: 67.57 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution mass spectrometry (DART+) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA.

Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 – 400 Mesh) purchased from Silicycle. Thin layer

chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), phosphomolybdic acid (PMA) in ethanol and ceric ammonium molybdate (CAM) in ethanol.

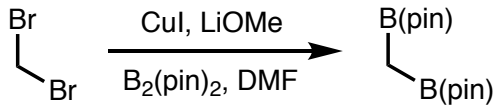
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether, dichloromethane and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon.

Bis(pinacolato)diboron was generously donated by Allychem Co., Ltd. and used without further purification. Triethylamine was purchased from Alfa Aesar and distilled over calcium hydride prior to use. The following reagents were purchased and used without purification: copper(I) iodide (CuI) (Aldrich), lithium 2,2,6,6-tetramethylpiperidide (LTMP) (Aldrich), sodium *tert*-butoxide (NaO*t*-Bu) (Strem), palmitic acid-1-^{13}C (Cambridge Isotope Laboratories), and *N*,*N*-dimethylformamide (DMF) (Acros). All other reagents were purchased from either Aldrich, Alfa Aesar or Acros and used without further purification.

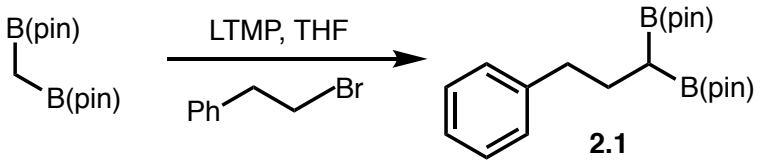
2.5.2 Representative Procedures for Preparation of *Geminal* Diboronate Esters

Method A:



In the glove box, an oven-dried 500 mL round-bottom flask with magnetic stir bar was charged with CuI (1.428 g, 7.500 mmol), LiOMe (8.543 g, 225 mmol) and $B_2(pin)_2$ (38.09 g, 150.0 mmol). The flask was sealed with a rubber septum, removed from the glove box, followed by the addition of DMF (150 mL) under N_2. After stirring at room temperature for 10 min, dibromomethane (10.53 mL, 150.0 mmol) was added *via* syringe at room temperature. The reaction mixture was allowed to stir at room temperature for 12 hours. Upon completion, 200 mL diethyl ether was added. The slurry was filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture in DMF was diluted with hexanes (300 mL), washed with H_2O (75 mL × 4), dried over Na_2SO_4, then concentrated *in vacuo*. The desired product bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane was obtained as a white solid (15.72 g, 78%) and used without further purification.

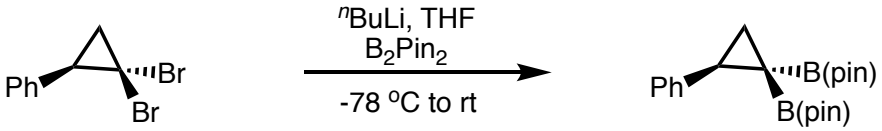
Method B:



2.1

In the glove box, an oven-dried 25 mL round-bottom flask with magnetic stir bar was charged with LTMP (773 mg, 5.25 mmol). The flask was sealed with a rubber septum, removed from the glove box, followed by the addition of THF (20 mL) under N_2. The reaction mixture was cooled to 0 ^oC, and a solution of 1,1-diborylmethane (1.34 g, 5.00 mmol) in THF (5 mL) was added *via* syringe and the mixture was allowed to stir at 0 °C for 10 minutes. (2-Bromoethyl)benzene (751 μL, 5.50 mmol) was added dropwise and the reaction was allowed to stir at 0 ^oC for 15 min. Upon completion, the reaction mixture was warmed to room temperature, filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 9:1) to afford the desired product **2.1** as a colorless oil (1.54 g, 83%).

Method C:



The *gem*-diboryl cyclopropane was prepared according to the literature procedure with some modification.[26] An oven-dried 25 mL round-bottom flask with magnetic stir bar was charged with $B_2(pin)_2$ (508 mg, 2.0 mmol) and (2,2-dibromocyclopropyl)benzene (607 mg, 2.20 mmol). The flask was sealed with a rubber septum and purged with N_2. THF (6 mL) was added and the reaction mixture was cooled to −78 ^oC. *n*-BuLi (2.50 M in hexanes, 0.88 mL, 2.20 mmol) was added dropwise and the reaction was allowed to stir at −78 ^oC for 10 min, then warmed to room temperature and stirred for 12 hours. The reaction mixture was quenched by H_2O at 0 ^oC, extracted with diethyl ether, dried over Na_2SO_4, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 9:1) to afford the desired product as a white solid (471 mg, 64%).

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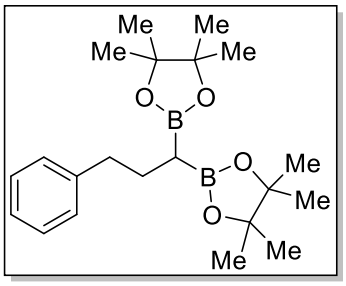
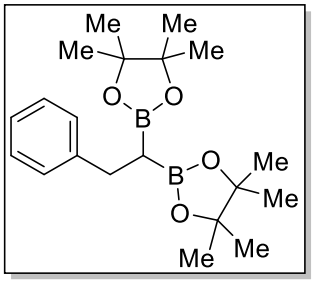
[26] Shimizu, M.; Schelper, M.; Nagao, I.; Shimono, K.; Kurahashi, T.; Hiyama, T. *Chem. Lett.* **2006**, 35, 1222-1223.

2.5.3 Full Characterization of *Geminal* Diboronate Esters



2,2'-(3-phenylpropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1, 3,2-dioxaborolane) (2.1). Prepared according to *Representative Procedure (Method B)*. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.23 (2H, m), 7.18-7.14 (3H, m), 2.60-2.57 (2H, m), 1.88-1.83 (2H, m), 1.24 (12H, s), 1.23 (12H, s), 0.81 (1H, t, J = 7.8 Hz). The ^{1}H NMR spectrum was in accord with previously reported data.[27]



2,2'-(2-phenylethane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.1). Prepared according to *Representative Procedure (Method B)* with LTMP (424 mg, 2.88 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (734 mg, 2.74 mmol), benzyl bromide (356 μL, 3.01 mmol), and THF (13 mL). The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 9:1) to afford the desired product as a colorless oil (753 mg, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25-7.20 (4H, m), 7.13-7.09 (1H, m), 2.88 (2H, d, J = 8.3 Hz), 1.20-1.15 (1H, m), 1.18 (12H, s), 1.17 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.5, 128.3, 128.0, 125.3, 83.1,

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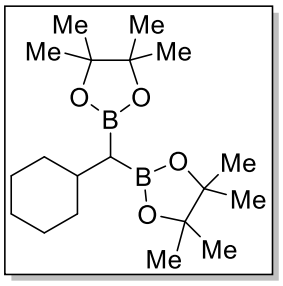
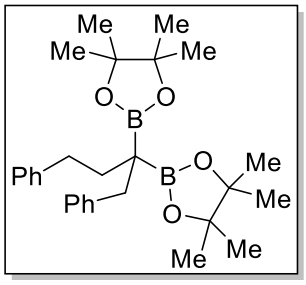
[27] Sun, C.; Porter, B.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 6534-6537.

31.3, 24.8, 24.5; IR (neat): 2976.9 (w), 2930.2 (w), 1454.0 (w), 1357.5 (m), 1311.7 (s), 1267.1 (m), 1135.9 (s), 969.6 (m), 850.9 (m), 732.2 (w), 697.6 (m), 528.3 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{20}{}^{1}H_{33}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 359.2565, found: 359.2565.

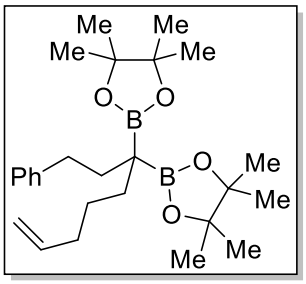


2,2'-(cyclohexylmethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.2). The reaction was performed according to *Representative Procedure (Method A)* with CuI (19.1 mg, 0.1 mmol), LiOMe (94.9 mg, 2.5 mmol), $B_2(pin)_2$ (508 mg, 2.0 mmol), (dibromomethyl) cyclohexane (313 mg, 1.2 mmol) and DMF (2 mL). The crude reaction mixture was purified by column chromatography on silica gel (10:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (239 mg, 68%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.78-1.57 (6H, m), 1.35-1.20 (2H, m), 1.23 (12H, s), 1.22 (12H, s), 1.12-1.04 (1H, m), 0.95-0.87 (2H, m), 0.64 (1H, d, J = 10.3 Hz). The ^{1}H NMR spectrum was in accord with previously reported data.[27]



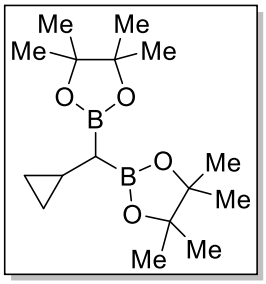
2,2'-(1,4-diphenylbutane-2,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.3). The reaction was performed according to *Representative Procedure (Method C)* with diboronate ester **2.1** (372 mg, 1.00 mmol), LTMP (155 mg,

1.05 mmol), benzyl bromide (131 μL, 1.10 mmol) and THF (5 mL). The crude reaction mixture was purified by column chromatography on silica gel (20:1 – 10:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (353 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.32 (2H, m), 7.24-7.19 (4H, m), 7.16-7.09 (4H, m), 3.08 (2H, s), 2.66-2.63 (2H, m), 1.82-1.79 (2H, m), 1.27 (12H, s), 1.23 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.5, 141.7, 129.7, 128.5, 128.1, 127.8, 125.6, 125.4, 83.3, 34.8, 33.9, 31.7, 25.1, 24.7; IR (neat): 2976.9 (w), 2926.6 (w), 1452.6 (m), 1350.0 (m), 1308.0 (s), 1247.6 (m), 1207.6 (m), 1134.4 (s), 967.8 (w), 848.6 (m), 698.0 (s), 578.9 (w), 492.7 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{28}{}^{1}H_{41}{}^{11}B_2{}^{16}O_4$ [M+H]: calculated: 463.3191, found: 463.3204.



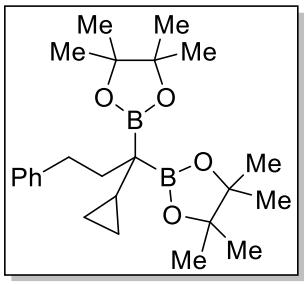
2,2'-(1-phenyloct-7-ene-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3, 2-dioxaborolane) (3.1). The reaction was performed according to *Representative Procedure (Method B)* with diboronate ester **2.1** (186 mg, 0.50 mmol), LTMP (77.3 mg, 0.525 mmol), 5-bromo-1-pentene (65 μL, 0.55 mmol) and THF (2.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (20:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (195.2 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.23 (2H, m), 7.20-7.19 (2H, m), 7.15-7.12 (1H, m), 5.86 (1H, ddt, J = 17.1, 10.3, 6.9 Hz),

5.01 (1H, ddt, J = 17.1, 2.0, 1.5 Hz), 4.93 (1H, ddt, J = 10.3, 2.4, 1.0 Hz), 2.52-2.49 (2H, m), 2.10-2.06 (2H, m), 1.91-1.88 (2H, m), 1.74-1.71 (2H, m), 1.41-1.35 (2H, m), 1.23 (24H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 139.3, 128.5, 128.1, 125.4, 114.0, 83.0, 34.5, 33.8, 31.9, 28.7, 26.6, 24.8, 24.7; IR (neat): 2975.6 (w), 2917.6 (w), 1354.0 (w), 1309.2 (s), 1249.5 (m), 1135.3 (s), 966.9 (w), 849.1 (m), 750.5 (w), 699.6 (m), 669.0 (w) cm^{-1}.

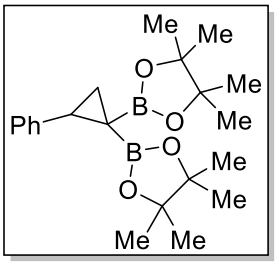


2,2'-(cyclopropylmethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.4). The reaction was performed according to *Representative Procedure (Method C)* with (dibromomethyl) cyclopropane (470.6 mg, 2.20 mmol), $B_2(pin)_2$ (508.0 mg, 2.00 mmol), *n*-BuLi (2.50 M, 0.88 mL, 2.20 mmol) and THF (6 mL). The crude reaction mixture was purified by column chromatography on silica gel (15:1 – 9:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (116.8 mg, 19%). The ^{1}H NMR spectrum was in accord with previously reported data.[28]

[28] Li, H.; Shangguan, X.; Zhang, Z.; Huang, S.; Zhang, Y.; Wang, J. *Org. Lett.* **2014**, *16*, 448-451.

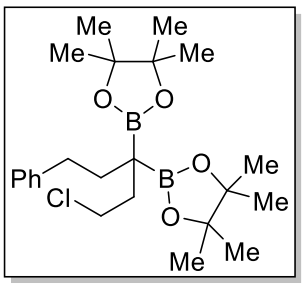


2,2'-(1-cyclopropyl-3-phenylpropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.5). The reaction was performed according to *Representative Procedure (Method B)* with diboronate ester **S2.4** (116.0 mg, 0.377 mmol), LiTMP (58.3 mg, 0.396 mmol), (2-bromoethyl)benzene (0.057 mL, 0.415 mmol) and THF (2 mL). The crude reaction mixture was purified by column chromatography on silica gel (30:1 – 20:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (116.2 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.21 (4H, m), 7.15-7.12 (1H, m), 2.73-2.70 (2H, m), 1.90-1.86 (2H, m), 1.22 (24H, s), 0.97-0.91 (1H, m), 0.46-0.38 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.2, 128.5, 128.1, 125.3, 82.8, 35.9, 34.8, 24.8, 24.7, 12.9, 3.6; IR (neat): 2977.0 (w), 1345.8 (m), 1311.2 (s), 1247.3 (m), 1213.1 (w), 1187.6 (w), 1131.8 (s), 967.6 (m), 848.2 (s), 826.2 (w), 757.5 (w), 741.6 (w), 699.8 (m), 668.5 (w), 601.8 (w), 494.2 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{24}{}^{1}H_{38}{}^{11}B_2{}^{16}O_4$ $[M]^{+\cdot}$: calculated: 412.2956, found: 412.2967.



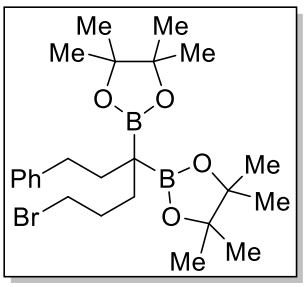
2,2'-(2-phenylcyclopropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.6). The reaction was performed according to *Representative Procedure (Method C)*. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25-7.23 (2H, m), 7.21-7.17 (2H, m),

7.12-7.08 (1H, m), 2.47 (1H, dd, J = 7.3, 5.9 Hz), 1.52 (1H, dd, J = 5.4, 3.4 Hz), 1.27-1.22 (1H, m), 1.222 (6H, s, overlap), 1.215 (6H, s, overlap), 0.99 (6H, s), 0.94 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.9, 128.3, 127.8, 125.8, 82.88, 82.86, 26.7, 24.83, 24.81, 24.7, 24.2, 14.1; IR (neat): 2977.5 (m), 2930.2 (w), 1379.1 (s), 1342.6 (s), 1298.8 (m), 1215.2 (w), 1148.2 (s), 1113.9 (m), 968.0 (w), 851.2 (m), 696.3 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{21}{}^{1}H_{33}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 371.2565, found: 371.2568.

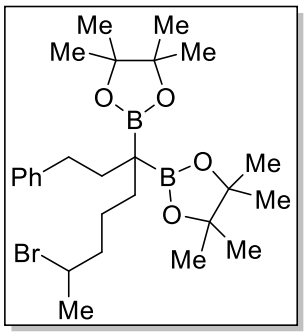


2,2'-(1-chloro-5-phenylpentane-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**S2.7**). The reaction was performed according to *Representative Procedure (Method B)* with diboronate ester **2.1** (186 mg, 0.50 mmol), LTMP (77.3 mg, 0.525 mmol), 1-bromo-2-chloro ethane (83 μL, 1.0 mmol) and THF (2.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (10:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (178 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.24 (2H, m), 7.19 (2H, d, J = 7.3 Hz), 7.15 (1H, t, J = 7.3 Hz), 3.62 (2H, t, J = 8.3 Hz), 2.57-2.53 (2H, m), 2.20 (2H, t, J = 8.3 Hz), 1.90-1.87 (2H, m), 1.23 (24H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.1, 128.4, 128.2, 125.6, 83.3, 43.5, 33.9, 33.1, 32.4, 24.8, 24.7; IR (neat): 2977.8 (m), 2931.0 (w), 2865.6 (w), 1454.9 (w), 1353.5 (m), 1317.0 (s), 1243.1 (m), 1137.0 (s), 967.5 (w), 852.1 (m), 699.6 (w) cm^{-1};

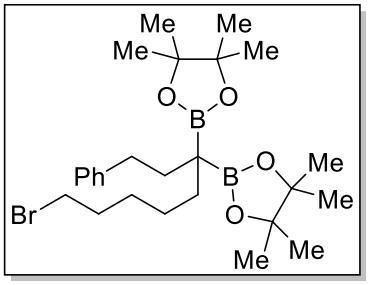
HRMS-(DART+) for $^{12}C_{23}{}^{1}H_{38}{}^{11}B_{2}{}^{35}Cl_{1}{}^{16}O_{4}$ $[M+H]^{+}$: calculated: 435.2645, found: 435.2665.



2,2'-(6-bromo-1-phenylhexane-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**S2.8**). The reaction was performed according to *Representative Procedure (Method B)* with diboronate ester **2.1** (186 mg, 0.50 mmol), LTMP (77.3 mg, 0.525 mmol), 1,3-dibromo propane (0.12 mL, 1.2 mmol) and THF (2.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (10:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (217 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.24 (2H, m), 7.20 (2H, d, J = 7.3 Hz), 7.14 (1H, t, J = 7.3 Hz), 3.42 (2H, t, J = 6.8 Hz), 2.54-2.51 (2H, m), 1.90-1.85 (4H, m), 1.81-1.78 (2H, m), 1.23 (24H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.5, 128.5, 128.2, 125.5, 83.2, 34.5, 33.8, 32.1, 30.9, 28.0, 24.8, 24.7; IR (neat): 2977.3 (m), 2930.7 (w), 2863.3 (w), 1454.7 (w), 1353.9 (m), 1308.9 (m), 1250.2 (m), 1213.8 (w), 11369 (s), 967.8 (w), 853.6 (m), 699.6 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{24}{}^{1}H_{40}{}^{11}B_{2}{}^{79}Br_{1}{}^{16}O_{4}$ $[M+H]^{+}$: calculated: 493.2296, found: 493.2309.

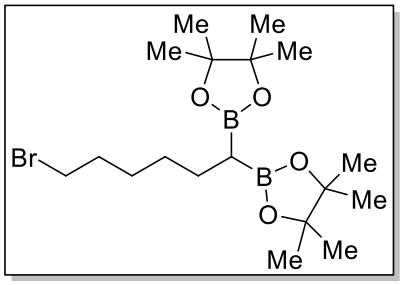


2,2'-(7-bromo-1-phenyloctane-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.9). The reaction was performed according to *Representative Procedure (Method B).* ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.23 (2H, m), 7.21-7.20 (2H, m), 7.16-7.12 (1H, m), 4.23-4.16 (1H, m), 2.57-2.46 (2H, m), 1.94-1.84 (3H, m), 1.81-1.64 (3H, m), 1.71 (3H, d, J = 6.8 Hz), 1.53-1.38 (2H, m), 1.24 (12H, s), 1.23 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.7, 128.5, 128.1, 125.4, 83.0, 52.0, 41.8, 33.8, 31.9, 28.3, 26.5, 25.3, 24.83, 24.79, 24.72, 24.70; IR (neat): 2979.3 (w), 2923.1 (w), 2862.9 (w), 1452.7 (w), 1304.5 (s), 1246.6 (m), 1137.1 (s), 968.4 (w), 860.1 (m), 743.1 (m), 696.6 (m), 668.0 (w), 522.7 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{26}{}^{1}H_{44}{}^{11}B_2{}^{79}Br_1{}^{16}O_4$ $[M+H]^+$: calculated: 521.2609, found: 521.2609.



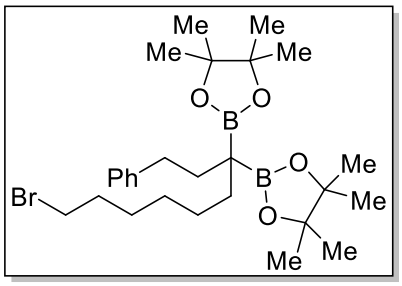
2,2'-(8-bromo-1-phenyloctane-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.10). The reaction was performed according to *Representative Procedure (Method B)* with diboronate ester **2.1** (372 mg, 1.00 mmol), LTMP (155 mg, 1.05 mmol), 1,5-dibromopentane (0.272 mL, 2.00 mmol) and THF (5 mL). The crude reaction mixture was purified by column chromatography on silica gel (15:1 – 10:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (436

mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.23 (2H, m), 7.20-7.19 (2H, m), 7.16-7.12 (1H, m), 3.42 (2H, t, *J* = 6.9 Hz), 2.52-2.49 (2H, m), 1.92-1.87 (4H, m), 1.72-1.69 (2H, m), 1.49-1.43 (2H, m), 1.36-1.27 (2H, m), 1.23 (24H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.7, 128.5, 128.1, 125.4, 83.0, 34.0, 33.8, 32.7, 31.9, 28.80, 28.75, 26.1, 24.8, 24.7; IR (neat): 2972.1 (w), 2929.4 (w), 2856.6 (w), 1451.9 (w), 1348.8 (m), 1307.4 (s), 1244.1 (s), 1133.9 (s), 1047.7 (w), 1020.2 (w), 968.4 (m), 848.5 (s), 754.2 (m), 699.8 (s), 666.9 (m), 558.0 (w), 502.6 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{26}{}^{1}H_{44}{}^{11}B_2{}^{79}Br_1{}^{16}O_4$ $[M+H]^+$: calculated: 521.2609, found: 521.2634.



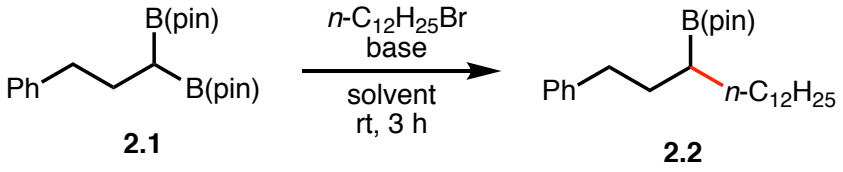
2,2'-(6-bromohexane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.11). The reaction was performed according to *Representative Procedure (Method B)* with bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (375 mg, 1.40 mmol), LTMP (216 mg, 1.47 mmol), 1,5-dibromopentane (0.245 mL, 1.80 mmol) and THF (7 mL). The crude reaction mixture was purified by column chromatography on silica gel (10:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (496 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.39 (2H, t, *J* = 7.1 Hz), 1.84 (2H, q, *J* = 7.3 Hz), 1.54 (2H, q, *J* = 7.8 Hz), 1.44-1.38 (2H, m), 1.35-1.27 (2H, m), 1.224 (12H, s), 1.216 (12H, s), 0.70 (1H, t,

J = 7.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 82.9, 33.9, 32.6, 31.4, 28.1, 25.3, 24.8, 24.5; IR (neat): 2976.6 (w), 2929.7 (w), 1462.6 (w), 1356.7 (m), 1307.8 (s), 1266.9 (m), 1234.5 (m), 1137.3 (s), 968.9 (m), 849.0 (m), 669.8 (w), 578.4 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{18}{}^{1}H_{36}{}^{11}B_2{}^{79}Br_1{}^{16}O_4$ $[M+H]^+$: calculated: 417.1983, found: 417.1975.



2,2'-(9-bromo-1-phenylnonane-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2.12). The reaction was performed according to *Representative Procedure (Method B)* with **2.1** (186 mg, 0.50 mmol), LTMP (77.3 mg, 0.525 mmol), 1,6-dibromohexane (154 μL, 1.0 mmol) and THF (2.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (10:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (206 mg, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.23 (2H, m), 7.19 (2H, d, J = 6.8 Hz), 7.14 (1H, t, J = 6.8 Hz), 3.41 (2H, t, J = 6.9 Hz), 2.52-2.49 (2H, m), 1.91-1.83 (4H, m), 1.71-1.68 (2H, m), 1.47-1.42 (2H, m), 1.36-1.23 (4H, m), 1.23 (24H, s, overlap); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 128.5, 128.1, 125.4, 83.0, 34.0, 33.8, 32.9, 31.9, 29.5, 28.9, 28.2, 26.9, 24.8, 24.7; IR (neat): 2976.8 (m), 2929.6 (m), 2857.4 (w), 1454.8 (w), 1306.6 (s), 1253.3 (m), 1137.2 (s), 968.3 (w), 853.8 (w), 749.7 (w), 699.4 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{27}{}^{1}H_{46}{}^{11}B_2{}^{79}Br_1{}^{16}O_4$ $[M+H]^+$: calculated: 535.2766, found: 535.2781.

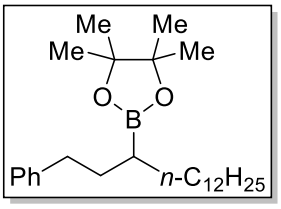
2.5.4 Representative Procedure for Deborylative Alkylation



2.1 **2.2**

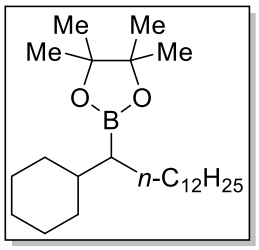
In the glove box, an oven-dried 2-dram vial with magnetic stir bar was charged with 1,1-diboronate ester **2.1** (48.4 mg, 0.13 mmol), 1-bromododecane (24.0 μL, 0.10 mmol) and THF (0.50 mL), followed by the NaO^{t}Bu (0.30 mmol). The vial was sealed with a polypropylene cap, removed from the glove box, and was allowed to stir at room temperature for 3 hours. Upon completion, the reaction mixture was diluted with diethyl ether (2 mL), filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 75:1) to afford the desired product **2.2** as a colorless oil.

2.5.5 Full Characterization of Deborylative Alkylation Products and Proof of Stereochemistry



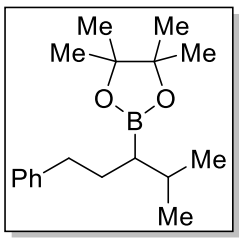
4,4,5,5-tetramethyl-2-(1-phenylpentadecan-3-yl)-1,3,2-dioxaborolane (2.2). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.25 (2H,

m), 7.19-7.14 (3H, m), 2.65-2.54 (2H, m), 1.78-1.70 (1H, m), 1.68-1.61 (1H, m), 1.47-1.34 (2H, m), 1.33-1.20 (32H, m), 1.07-1.01 (1H, m), 0.88 (3H, t, J = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.2, 128.4, 128.2, 125.5, 82.9, 35.7, 33.5, 31.9, 31.3, 29.9, 29.70, 29.67, 29.65, 29.61, 29.59, 29.4, 29.2, 24.9, 24.8, 22.7, 14.1; IR (neat): 2976.6 (w), 2921.8 (s), 2852.4 (m), 1456.1 (w), 1385.8 (m), 1314.5 (m), 1143.4 (s), 966.5 (w), 746.5 (w), 698.0 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{27}{}^{1}H_{48}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^+$: calculated: 415.3747, found: 415.3744.

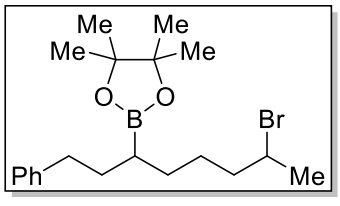


2-(1-cyclohexyltridecyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.13). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with 1,1-diboronate ester **S2.2** (45.5 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), 1-bromododecane (24.0 μL, 0.10 mmol) and THF (0.5 mL) at 40 °C for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (100:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (34.3 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.77-1.60 (5H, m), 1.43-0.81 (44H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 82.7, 39.7, 32.9, 32.6, 31.9, 30.0, 29.70, 29.68, 29.66, 29.64, 29.62, 29.60, 29.4, 28.8, 26.8, 25.0, 24.8, 22.7, 14.1; IR (neat): 2977.4 (w), 2920.9 (s), 2851.6 (m), 1447.8 (w), 1378.7 (m), 1312.4 (m), 1238.0 (w), 1144.8 (m), 970.9 (w), 865.3 (w) cm^{-1};

HRMS-(DART+) for $^{12}C_{25}{}^{1}H_{53}{}^{11}B_{1}{}^{14}N_{1}{}^{16}O_{2}$ $[M+NH_4]^+$: calculated: 410.4169, found: 410.4175.

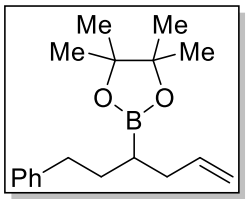


4,4,5,5-tetramethyl-2-(4-methyl-1-phenylpentan-3-yl)-1,3,2-dioxaborolane (2.4). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with 1,1-diboronate ester **2.1** (48.4 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), 2-bromopropane (9.4 μL, 0.10 mmol) and THF (0.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (75:1 – 50:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (21.7 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.25 (2H, m), 7.20-7.14 (3H, m), 2.67-2.61 (1H, m), 2.54-2.48 (1H, m), 1.80-1.72 (2H, m), 1.70-1.63 (1H, m), 1.28 (12H, s), 0.94-0.90 (7H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.2, 128.4, 128.2, 125.5, 82.9, 36.0, 31.4, 29.6, 25.1, 24.9, 22.3, 21.7; IR (neat): 2976.7 (w), 2955.3 (w), 2929.6 (w), 2867.2 (w), 1454.7 (w), 1379.4 (m), 1314.1 (m), 1213.4 (w), 1143.1 (s), 967.5 (w), 848.2 (w), 747.9 (w), 698.5 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{18}{}^{1}H_{30}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^+$: calculated: 289.2339, found: 289.2353.



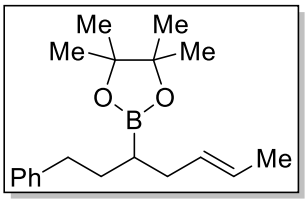
2-(7-bromo-1-phenyloctan-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.5). The reaction was performed

according to *Representative Procedure for Deborylative Alkylation* with 1,1-diboronate ester **S2.9** (48.4 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), 1,4-dibromopentane (13.6 μL, 0.10 mmol) and THF (0.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (25:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (39.4 mg, mixture of the desired product (1:1 dr) and $Ph(CH_2)_3B(pin)$, 3.3:1, calculated yield = 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.24 (2H, m), 7.19-7.15 (3H, m), 4.16-4.09 (1H, m), 2.66-2.54 (2H, m), 1.87-1.61 (4H, m), 1.69 (3H, dd, *J* = 6.4, 1.5 Hz, overlap), 1.57-1.34 (4H, m), 1.27 (12H, s), 1.08-1.03 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.9, 128.4, 128.2, 125.6, 83.0, 51.84, 51.79, 41.4, 41.3, 35.6, 33.40, 33.37, 30.52, 30.51, 27.3, 27.2, 26.4, 24.88, 24.87, 24.85; IR (neat): 2976.9 (w), 2926.0 (w), 2858.0 (w), 1454.0 (w), 1378.4 (m), 1316.5 (m), 1213.4 (m), 1143.0 (s), 966.3 (w), 853.5 (w), 746.8 (w), 698.9 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{20}{}^{1}H_{33}{}^{11}B_1{}^{79}Br_1{}^{16}O_2$ $[M+H]^+$: calculated: 395.1757, found: 395.1757.



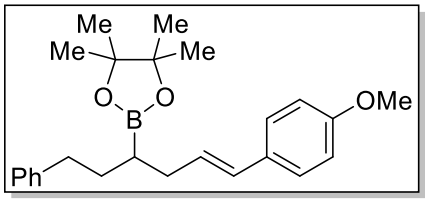
4,4,5,5-tetramethyl-2-(1-phenylhex-5-en-3-yl)-1,3,2-dioxaborolane (2.6). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with 1,1-diboronate ester **2.1** (96.7 mg, 0.26 mmol), NaO*t*-Bu (57.7 mg, 0.60 mmol), allyl chloride (16.3 μL, 0.20 mmol) and THF (1.0 mL). The crude reaction mixture was purified by column

chromatography on silica gel (50:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (49.7 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.25 (2H, m), 7.19-7.15 (3H, m), 5.81 (1H, ddt, *J* = 17.1, 10.3, 6.9 Hz), 5.02 (1H, app dq, *J* = 17.1, 2.0 Hz), 4.94 (1H, app dt, *J* = 10.3, 1.0 Hz), 2.67-2.56 (2H, m), 2.26-2.14 (2H, m), 1.79-1.72 (1H, m), 1.71-1.63 (1H, m), 1.26 (12H, s), 1.18-1.12 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.9, 138.4, 128.4, 128.2, 125.6, 114.9, 83.1, 35.4, 35.3, 32.9, 24.9, 24.8; IR (neat): 2977.0 (w), 2924.5 (w), 2857.2 (w), 1453.9 (w), 1379.8 (m), 1317.8 (m), 1242.3 (w), 1142.7 (s), 966.8 (w), 908.9 (w), 862.8 (w), 747.1 (w), 698.5 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{18}{}^{1}H_{28}{}^{11}B_{1}{}^{16}O_2$ $[M+H]^+$: calculated: 287.2182, found: 287.2178.



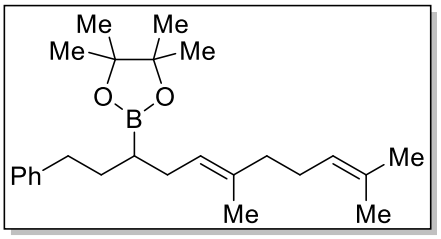
(*E*)-4,4,5,5-tetramethyl-2-(1-phenylhept-5-en-3-yl)-1,3,2-dioxaborolane (2.7). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with **2.1** (48.4 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), crotyl chloride (9.8 μL, 0.10 mmol, 5.8:1 *E*/*Z* isomers) and THF (0.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (50:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (27.9 mg, 93%, 6.0:1 *E*/Z, determined by oxidizing the boronate ester to the corresponding alcohol)**.** ^{1}H NMR (500 MHz, $CDCl_3$) (mixture of *E*/*Z* isomers): δ 7.28-7.25 (2H, m), 7.19-7.14 (3H, m), 5.47-5.37 (2H, m), 2.65-2.55 (2H, m),

2.43-2.08 (2H, m), 1.78-1.70 (1H, m), 1.69-1.61 (4H, m), 1.25 (12H, s), 1.14-1.08 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) (mixture of *E*/*Z* isomers): δ 143.0, 130.9, 130.2, 128.4, 128.2, 125.5, 125.3, 124.1, 83.01, 82.96, 35.6, 35.5, 34.2, 33.04, 33.02, 28.3, 24.88, 24.81, 24.77, 17.8, 12.9; IR (neat): 2977.1 (w), 2924.7 (w), 2855.5 (w), 1453.3 (w), 1379.8 (m), 1317.1 (m), 1238.3 (w), 1143.3 (s), 965.9 (m), 862.1 (w), 746.8 (w), 698.5 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{18}{}^{1}H_{28}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^+$: calculated: 287.2182, found: 287.2178.



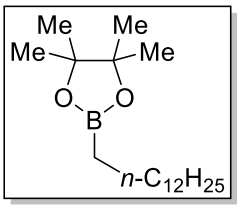
(*E*)-2-(6-(4-methoxyphenyl)-1-phenylhex-5-en-3-yl) -4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.8). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with 1,1-diboronate ester **2.1** (48.4 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), (*E*)-1-(3-chloroprop-1-en-1-yl)-4-methoxybenzene (18.3 mg, 0.10 mmol) and THF (0.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (20:1 – 10:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (28.3 mg, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.24 (4H, m), 7.19-7.15 (3H, m), 6.84-6.81 (2H, m), 6.34 (1H, d, J = 15.7 Hz), 6.07 (1H, dt, J = 15.7, 7.3 Hz), 3.80 (3H, s), 2.70-2.59 (2H, m), 2.38-2.28 (2H, m), 1.84-1.77 (1H, m), 1.75-1.68 (1H, m), 1.25 (6H, s), 1.24 (6H, s), 1.29-1.21 (1H, m, overlap); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.6, 142.9, 130.8, 129.7,

128.4, 128.3, 128.2, 127.0, 125.6, 113.8, 83.1, 55.2, 35.5, 34.6, 33.1, 24.88, 24.87; IR (neat): 2976.6 (w), 2925.8 (w), 1607.0 (w), 1510.2 (s), 1454.8 (w), 1380.7 (m), 1319.4 (m), 1246.6 (s), 1173.9 (w), 1143.0 (s), 1035.9 (w), 965.6 (w), 848.4 (w), 699.6 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{25}{}^{1}H_{33}{}^{11}B_{1}{}^{16}O_{3}$ $[M]^{+\cdot}$: calculated: 392.2523, found: 392.2540.

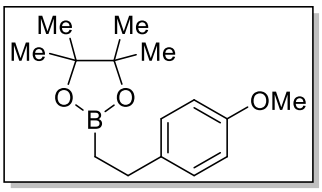


(*E*)-2-(6,10-dimethyl-1-phenylundeca-5,9-dien-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.9). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with 1,1-diboronate ester **2.1** (48.4 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), geranyl chloride (18.5 μL, 0.10 mmol) and THF (0.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (50:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (34.8 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.24 (2H, m), 7.19-7.14 (3H, m), 5.15-5.08 (2H, m), 2.66-2.55 (2H, m), 2.19-2.10 (2H, m), 2.08-2.04 (2H, m), 1.98-1.95 (2H, m), 1.79-1.63 (2H, m), 1.67 (3H, d, J = 1.0 Hz, overlap), 1.61 (3H, s), 1.59 (3H, s), 1.25 (12H, s), 1.13-1.08 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.1, 135.1, 131.2, 128.4, 128.2, 125.5, 124.4, 124.1, 82.9, 39.8, 35.6, 33.1, 29.4, 26.7, 25.7, 24.9, 24.8, 17.6, 16.2; IR (neat): 2976.2 (m), 2923.8 (m), 2855.3 (w), 1453.0 (w), 1379.8 (m), 1317.6 (m), 1240.9 (w), 1143.8 (s), 967.3 (w), 866.9 (w),

746.3 (w), 698.5 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{25}{}^{1}H_{40}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 383.3121, found: 383.3136.

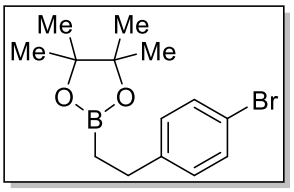


4,4,5,5-tetramethyl-2-tridecyl-1,3,2-dioxaborolane (2.10). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (53.6 mg, 0.20 mmol), KO*t*-Bu (56.1 mg, 0.50 mmol), 1-bromododecane (24.0 μL, 0.10 mmol) and toluene (0.5 mL) at room temperature for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (75:1 – 50:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (28.2 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.41-1.37 (2H, m), 1.31-1.24 (30H, m), 0.88 (3H, t, J = 6.9 Hz), 0.76 (2H, t, J = 7.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 82.8, 32.4, 31.9, 29.70, 29.68, 29.66, 29.65, 29.59, 29.41, 29.35, 24.8, 24.0, 22.7, 14.1; IR (neat): 2977.8 (w), 2922.1 (s), 2853.1 (m), 1465.8 (w), 1376.7 (s), 1316.8 (m), 1145.9 (s), 968.4 (w), 847.0 (w), 720.6 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{19}{}^{1}H_{40}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 311.3121, found: 311.3121.



2-(4-methoxyphenethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.11). The reaction was performed according to

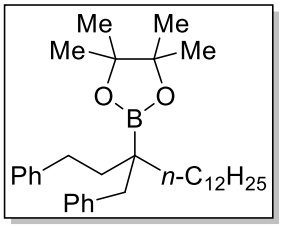
Representative Procedure for Deborylative Alkylation with bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (53.6 mg, 0.20 mmol), KO*t*-Bu (56.1 mg, 0.50 mmol), 4-methoxybenzyl chloride (13.6 μL, 0.10 mmol) and toluene (0.5 mL) at room temperature for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (20:1 – 10:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (19.2 mg, 73%). ^{1}H NMR was in accord with literature.[29]



2-(4-bromophenethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.12). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (53.6 mg, 0.20 mmol), KO*t*-Bu (56.1 mg, 0.50 mmol), 4-bromobenzyl chloride (20.5 mg, 0.10 mmol) and toluene (0.5 mL) at room temperature for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (20:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (23.9 mg, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.35 (2H, m), 7.10-7.07 (2H, m), 2.69 (2H, t, J = 8.1 Hz), 1.22 (12H, s), 1.11 (2H, t, J = 8.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.3, 131.2, 129.8, 119.2, 83.2, 29.4, 24.8; IR (neat):

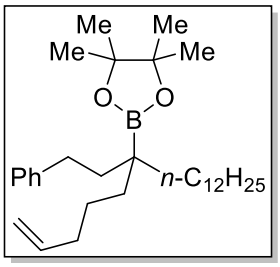
[29] Yamamoto, Y.; Fujikawa, R.; Umemoto, T.; Miyaura, N. *Tetrahedron*, **2004**, *60*, 10695-10700.

2977.4 (w), 2930.8 (w), 1487.4 (m), 1369.5 (s), 1315.5 (s), 1239.1 (w), 1141.9 (s), 1071.6 (m), 1010.7 (m), 966.8 (m), 866.8 (w), 849.2 (m), 798.1 (m), 672.3 (w), 484.1 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{14}{}^{1}H_{21}{}^{11}B_{1}{}^{79}Br_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 311.0819, found: 311.0811.

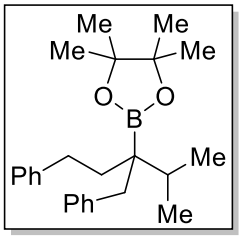


2-(3-benzyl-1-phenylpentadecan-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.15). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.3** (60.1 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), 1-bromododecane (24.0 μL, 0.10 mmol) and THF (0.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (50:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (49.9 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.22 (6H, m), 7.18-7.14 (4H, m), 2.80 (1H, d, J = 13.7 Hz), 2.76 (1H, d, J = 13.7 Hz), 2.64-2.60 (2H, m), 1.68-1.58 (2H, m), 1.45-1.36 (4H, m), 1.32-1.21 (30H, m), 0.89 (3H, t, J = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.5, 140.0, 130.2, 128.3, 128.2, 127.8, 125.7, 125.5, 83.2, 40.2, 36.7, 34.5, 31.9, 31.5, 30.5, 29.72, 29.68, 29.4, 25.15, 25.10, 24.8, 22.7, 14.1; IR (neat): 2976.9 (w), 2924.7 (s), 2853.3 (m), 1495.4 (w), 1456.2 (w), 1380.2 (m), 1311.3 (m), 1143.7 (m), 855.3 (w),

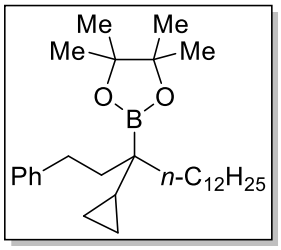
735.4 (w), 699.7 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{34}{}^{1}H_{54}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 505.4217, found: 505.4237.



4,4,5,5-tetramethyl-2-(6-phenethyloctadec-1-en-6-yl)-1,3,2-dioxaborolane (**2.16**). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **3.1** (57.2 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), 1-bromododecane (24.0 μL, 0.10 mmol) and THF (0.5 mL) at 50 °C for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (100:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (44.0 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.24 (2H, m), 7.19-7.14 (3H, m), 5.84 (1H, ddt, *J* = 17.1, 10.3, 6.9 Hz), 5.01 (1H, ddt, *J* = 17.1, 2.0, 1.5 Hz), 4.94 (1H, ddt, *J* = 10.3, 2.0, 1.5 Hz), 2.50-2.47 (2H, m), 2.05 (2H, q, *J* = 7.0 Hz), 1.66-1.62 (2H, m), 1.45-1.19 (26H, m), 1.25 (12H, s, overlap), 0.88 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 139.2, 128.3, 128.2, 125.4, 114.2, 83.0, 36.7, 34.7, 34.4, 33.8, 31.9, 31.4, 30.6, 29.72, 29.68, 29.65, 29.4, 24.9, 24.7, 24.2, 22.7, 14.1; IR (neat): 2922.9 (s), 2852.7 (m), 1458.2 (w), 1385.2 (m), 1345.1 (w), 1305.9 (m), 1260.9 (w), 1142.6 (s), 966.6 (w), 908.0 (w), 857.4 (w), 744.7 (w), 696.2 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{32}{}^{1}H_{56}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 483.4373, found: 483.4384.

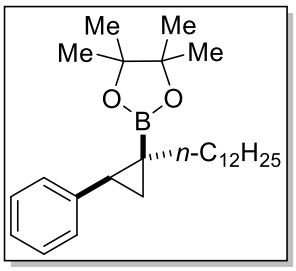


2-(3-benzyl-4-methyl-1-phenylpentan-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.14). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.3** (60.1 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), 2-bromopropane (9.4 μL, 0.10 mmol) and THF (0.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (100:1 – 75:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (35.9 mg, 95%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (2H, d, J = 7.3 Hz), 7.26-7.22 (4H, m), 7.18-7.10 (4H, m), 3.09 (1H, d, J = 13.7 Hz), 2.68 (1H, d, J = 14.2 Hz), 2.65-2.55 (2H, m), 1.78 (1H, sp, J = 6.8 Hz), 1.70-1.60 (2H, m), 1.28 (6H, s), 1.24 (6H, s), 1.06 (3H, d, J = 6.8 Hz), 0.99 (3H, d, J = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 140.8, 130.5, 128.4, 128.2, 127.7, 125.6, 125.4, 83.2, 37.9, 34.5, 32.4, 31.2, 25.4, 25.0, 19.6, 19.2; IR (neat): 2975.2 (w), 2930.7 (w), 2870.3 (w), 1455.1 (w), 1380.6 (m), 1305.3 (m), 1257.7 (m), 1139.7 (s), 973.7 (w), 846.7 (w), 738.4 (m), 699.9 (s), 670.6 (w), 502.6 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{25}{}^{1}H_{36}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^+$: calculated: 379.2808, found: 379.2804.



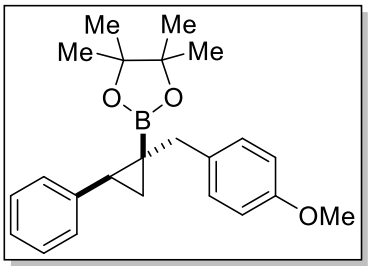
2-(3-cyclopropyl-1-phenylpentadecan-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.18). The reaction was performed according to *Representative Procedure for Deborylative*

Alkylation with diboronate ester **S2.5** (53.6 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), 1-bromododecane (24.0 μL, 0.10 mmol) and THF (0.5 mL) at 50 °C for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (200:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (25.3 mg, 56%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.25 (2H, m), 7.22-7.20 (2H, m), 7.17-7.14 (1H, m), 2.68-2.62 (2H, m), 1.77-1.71 (1H, m), 1.67-1.60 (1H, m), 1.46-1.42 (2H, m), 1.37-1.26 (20H, m), 1.22 (12H, s), 0.88 (3H, t, J = 6.9 Hz), 0.65-0.59 (1H, m), 0.43-0.30 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.3, 128.4, 128.2, 125.3, 82.8, 39.1, 36.4, 32.2, 31.9, 30.7, 29.72, 29.69, 29.66, 29.4, 25.4, 24.9, 22.7, 18.0, 14.1, 2.3, 1.9; IR (neat): 2922.9 (s), 2852.6 (m), 1455.7 (w), 1388.5 (w), 1370.8 (w), 1302.7 (m), 1142.8 (s), 1016.8 (w), 967.5 (w), 855.6 (w), 748.1 (w), 697.9 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{30}{}^{1}H_{52}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 455.4060, found: 455.4080.



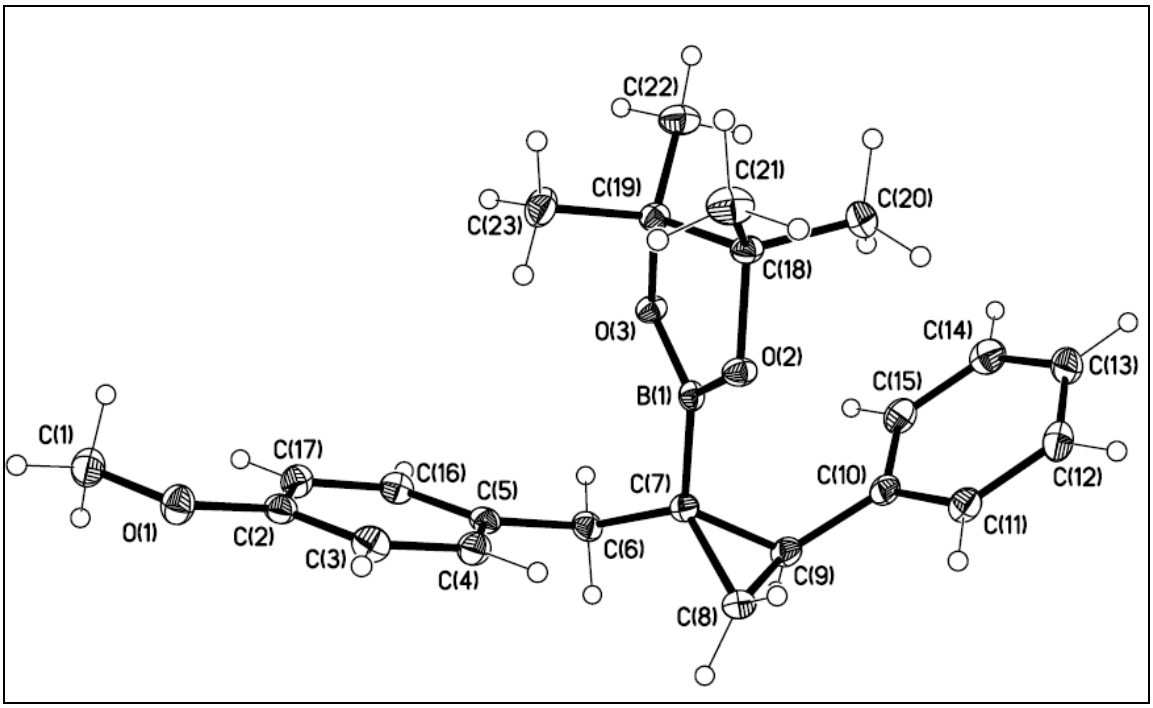
2-(1-dodecyl-2-phenylcyclopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.17). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.6** (48.1 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), 1-bromododecane (24.0 μL, 0.10 mmol) and THF (0.5 mL) at 60 °C for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel

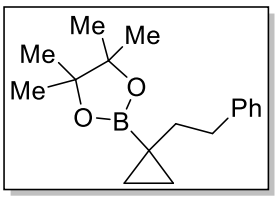
(50:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (26.8 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24-7.23 (2H, m), 7.20-7.17 (2H, m), 7.11-7.07 (1H, m), 1.98-1.93 (2H, m), 1.51-1.35 (3H, m), 1.32-1.25 (18H, m), 0.97 (6H, s), 0.93-0.88 (1H, m), 0.88 (3H, t, J = 6.8 Hz, overlap), 0.83 (6H, s), 0.77 (1H, dd, J = 7.3, 4.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.7, 128.8, 127.6, 125.5, 82.8, 38.4, 31.9, 29.9, 29.8, 29.72, 29.69, 29.66, 29.63, 29.4, 29.3, 24.7, 24.3, 22.7, 15.7, 14.1; IR (neat): 2977.1 (w), 2923.0 (s), 2852.9 (m), 1447.0 (w), 1408.4 (m), 1371.1 (m), 1312.7 (m), 1141.3 (s), 856.3 (w), 694.8 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{27}{}^{1}H_{46}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 413.3591, found: 413.3612. The relative stereochemistry was assigned by analogy.



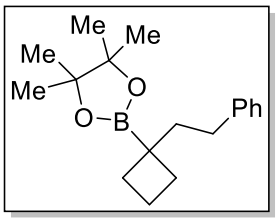
2-(1-(4-methoxybenzyl)-2-phenylcyclopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.19). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.6** (48.1 mg, 0.13 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol), 4-methoxybenzyl chloride (13.6 μL, 0.10 mmol) and THF (0.5 mL) at 50 °C for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (25:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (26.8 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.19 (6H, m), 7.12-7.09 (1H, m), 6.82-6.79 (2H, m), 3.79 (3H, s), 3.37 (1H, d, J = 14.2 Hz),

2.20 (1H, d, *J* = 14.7 Hz), 2.09 (1H, dd, *J* = 7.8, 5.9 Hz), 1.55 (1H, t, *J* = 4.9 Hz), 1.00 (1H, dd, *J* = 8.3, 4.4 Hz), 0.88 (6H, s), 0.73 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.8, 140.3, 133.8, 129.9, 128.8, 127.7, 125.7, 113.4, 83.0, 55.2, 42.0, 29.3, 24.6, 24.3, 15.6. IR (neat): 2978.5 (w), 2910.8 (w), 1609.2 (w), 1510.6 (s), 1442.4 (w), 1407.1 (m), 1315.4 (m), 1300.9 (m), 1248.4 (s), 1130.1 (s), 1029.8 (m), 967.9 (w), 852.3 (w), 770.2 (w), 691.6 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{23}{}^{1}H_{30}{}^{11}B_{1}{}^{16}O_{3}$ $[M+H]^{+}$: calculated: 365.2288, found: 365.2285. The relative stereochemistry was assigned by X-ray crystallography.



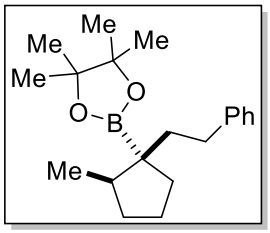


4,4,5,5-tetramethyl-2-(1-phenethylcyclopropyl)-1,3,2-dioxaborolane (2.20). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.7** (43.5 mg, 0.10 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol) and THF (0.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (20:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (25.4 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.24 (2H, m), 7.19-7.13 (3H, m), 2.74-2.71 (2H, m), 1.54-1.50 (2H, m), 1.22 (12H, s), 0.67-0.66 (2H, m), 0.30-0.28 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.2, 128.4, 128.1, 125.4, 82.9, 38.7, 35.8, 24.7, 11.5; IR (neat): 2977.8 (w), 2926.6 (w), 1453.5 (w), 1416.9 (s), 1371.1 (w), 1311.8 (m), 1193.8 (m), 1132.8 (s), 967.6 (w), 858.9 (w), 698.9 (m), 684.2 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{17}{}^{1}H_{26}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 273.2026, found: 273.2035.



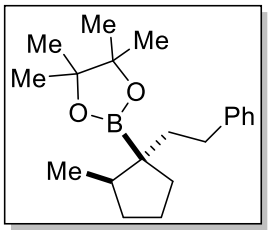
4,4,5,5-tetramethyl-2-(1-phenethylcyclobutyl)-1,3,2-dioxaborolane (2.21). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.8** (49.3 mg, 0.10 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol) and THF (0.5 mL) at room temperature for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (75:1 hexanes/diethyl ether, stain in CAM) to

afford a colorless oil (25.0 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.25 (2H, m), 7.20-7.14 (3H, m), 2.50-2.47 (2H, m), 2.18-2.13 (2H, m), 1.99-1.84 (4H, m), 1.736-1.70 (2H, m), 1.29 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.3, 128.3, 128.2, 125.5, 83.0, 42.0, 33.3, 30.2, 24.7, 18.2; IR (neat): 3026.0 (w), 2975.2 (m), 2929.5 (m), 2854.5 (w), 1454.1 (w), 1371.5 (s), 1343.3 (w), 1211.3 (m), 1142.6 (s), 965.1 (w), 860.7 (w), 698.3 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{18}{}^{1}H_{28}{}^{11}B_{1}{}^{16}O_2$ $[M+H]^+$: calculated: 287.2182, found: 287.2179.

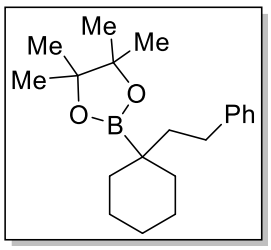


4,4,5,5-tetramethyl-2-(2-methyl-1-phenethylcyclopentyl)-1,3,2-dioxaborolane (2.22, major diastereomer). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.9** (208.5 mg, 0.40 mmol), NaO*t*-Bu (115.3 mg, 1.20 mmol) and THF (2.0 mL) at 50 °C for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (50:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (95.7 mg, 76%, 7.5:1 dr). The diastereomers were separated by a second column (75:1 hexanes/diethyl ether). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (2H, t, J = 7.3 Hz), 7.21 (2H, d, J = 7.3 Hz), 7.18-7.15 (1H, m), 2.58-2.49 (2H, m), 2.04 (1H, sx, J = 7.3 Hz), 1.89-1.83 (1H, m), 1.79-1.54 (5H, m), 1.44-1.36 (1H, m), 1.31-1.24 (1H, m), 1.27 (12H, s, overlap), 0.91 (3H, dd, J = 7.3,

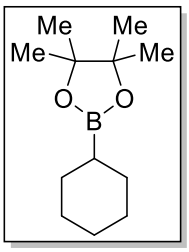
1.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.9, 128.3, 128.2, 125.4, 82.9, 40.3, 34.2, 33.5, 33.1, 32.6, 24.9, 24.6, 22.9, 15.1; IR (neat): 2949.5 (m), 2868.7 (w), 1454.3 (w), 1380.5 (s), 1304.3 (s), 1195.0 (w), 1143.5 (s), 967.1 (w), 856.4 (w), 747.3 (w), 698.3 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{20}{}^{1}H_{32}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^+$: calculated: 315.2495, found: 315.2500.



4,4,5,5-tetramethyl-2-(2-methyl-1-phenethylcyclopentyl)-1,3,2-dioxaborolane (2.22, minor diastereomer). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.25(2H, m), 7.20 (2H, d, *J* = 7.3 Hz), 7.16 (1H, t, *J* = 7.3 Hz), 2.59-2.53 (2H, m), 2.05-1.95 (2H, m), 1.84-1.78 (1H, m), 1.77-1.70 (1H, m), 1.64-1.56 (2H, m), 1.40-1.22 (3H, m), 1.27 (12H, s, overlap), 1.00 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.9, 128.3, 128.2, 125.4, 82.9, 45.0, 41.2, 34.26, 34.23, 34.15, 25.3, 24.8, 22.7, 17.8; IR (neat): 2976.1 (w), 2928.4 (m), 2856.0 (w), 1454.3 (w), 1387.4 (m), 1297.8 (m), 1200.8 (w), 1142.3 (s), 965.6 (w), 856.9 (w), 747.5 (w), 697.8 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{20}{}^{1}H_{32}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^+$: calculated: 315.2495, found: 315.2502.

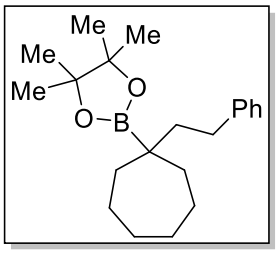


4,4,5,5-tetramethyl-2-(1-phenethylcyclohexyl)-1,3,2-dioxaborolane (2.24). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.10** (52.1 mg, 0.10 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol) and THF (0.5 mL) at 50 ^{o}C for 14 hours. The crude reaction mixture was purified by column chromatography on silica gel (75:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (21.8 mg, 69%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.24 (2H, m), 7.17-7.14 (3H, m), 2.58-2.54 (2H, m), 1.95 (2H, d, *J* = 12.7 Hz), 1.68-1.60 (3H, m), 1.58-1.54 (2H, m), 1.37-1.26 (2H, m), 1.29 (12H, s), 1.19-1.14 (1H, m), 0.99 (2H, td, *J* = 12.7, 2.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.7, 128.3, 128.2, 125.5, 83.0, 43.3, 35.3, 32.2, 26.7, 25.2, 24.9; IR (neat): 2977.3 (w), 2924.9 (s), 2850.6 (w), 1453.3 (w), 1387.7 (m), 1337.2 (w), 1304.6 (s), 1234.0 (m), 1143.1 (s), 968.5 (w), 696.5 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{20}{}^{1}H_{32}{}^{11}B_{1}{}^{16}O_2$ $[M+H]^+$: calculated: 315.2495, found: 315.2496.



2-cyclohexyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.23). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.11** (116.8 mg, 0.40 mmol), NaO*t*-Bu (115.3 mg, 1.20 mmol) and THF (2.0 mL). The crude reaction mixture was purified by column chromatography on silica gel (100:1

pentane/diethyl ether, stain in CAM) to afford a colorless oil (50.4 mg, 60%). The ^{1}H and ^{13}C NMR spectra were in accord with previously reported data.[30]



4,4,5,5-tetramethyl-2-(1-phenethylcycloheptyl)-1,3,2-dioxaborolane (2.25). The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with diboronate ester **S2.12** (53.5 mg, 0.10 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol) and THF (0.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (100:1 hexanes/ diethyl ether, stain in CAM) to afford a colorless oil (19.1 mg, 58%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.25 (2H, m), 7.18-7.14 (3H, m), 2.56-2.53 (2H, m), 1.91-1.86 (2H, m), 1.63-1.58 (4H, m), 1.56-1.44 (6H, m), 1.36-1.32 (2H, m), 1.27 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.7, 128.3, 128.2, 125.4, 82.9, 42.7, 36.2, 33.0, 29.7, 24.9, 24.6; IR (neat): 2976.9 (w), 2918.6 (m), 2851.0 (w), 1458.4 (w), 1386.5 (m), 1304.1 (m), 1263.3 (w), 1141.7 (s), 966.0 (w), 853.4 (m), 746.9 (w), 697.6 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{21}{}^{1}H_{34}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 329.2652, found: 329.2653.

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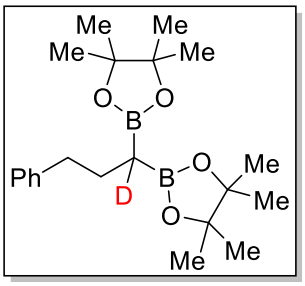
[30] Clary, J. W.; Rettenmaier, T. J.; Snelling, R.; Bryks, W.; Banwell, J.; Wipke, W. T.; Singaram, B. *J. Org. Chem.* **2011**, *76*, 9602-9610.

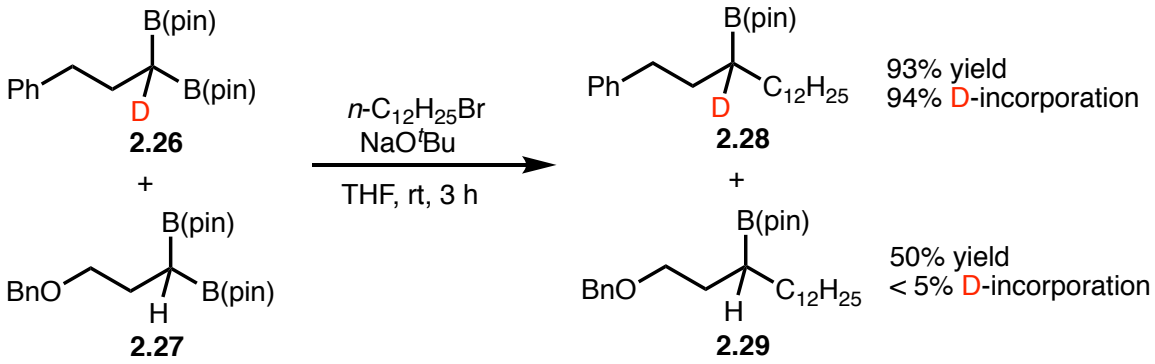
2.5.6 Procedure for Deborylative Alkylation Crossover Experiment:

In the glove box, an oven-dried 10 mL round-bottom flask with magnetic stir bar was charged with lithium 2,2,6,6-tetramethylpiperidide (125 mg, 0.85 mmol). The flask was sealed with a rubber septum, removed from the glove box, followed by the addition of THF (2.5 mL) under N_2. The reaction mixture was cooled to 0 ^oC, and a solution of 1,1-diboronate ester **2.1** (264 mg, 0.71 mmol) in THF (1 mL) was added *via* syringe and the mixture was allowed to stir at 0 °C for 10 minutes. D_2O (26 μL, 1.42 mmol) was added in one portion and the reaction was allowed to stir at 0 ^oC for 10 min. Upon completion, the reaction mixture was warmed to room temperature, filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 9:1) to afford the desired product as a white solid (206 mg, 78%).

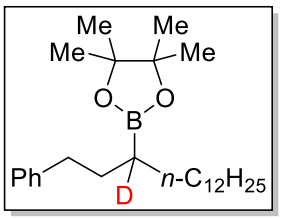


2,2'-(3-phenylpropane-1,1-diyl-1-*d*)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.26). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.23 (2H, m), 7.18-7.12 (3H, m), 2.60-2.57 (2H, m), 1.86-1.83 (2H, m), 1.24 (12H, s), 1.23 (12H, s);

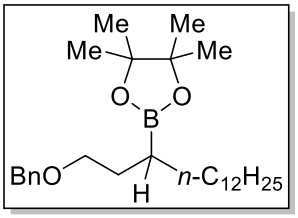
HRMS-(DART+) for $^{12}C_{21}{}^{1}H_{34}{}^{2}H_{1}{}^{11}B_{2}{}^{16}O_{4}$ $[M+H]^{+}$: calculated: 374.2784, found: 374.2781.



In the glove box, an oven-dried 2-dram vial with magnetic stir bar was charged with deuterated 1,1-diboronate ester **2.26** (48.5 mg, 0.13 mmol), **2.27** (52.3 mg, 0.13 mmol), NaO*t*-Bu (57.7 mg, 0.60 mmol), and THF (0.50 mL). The reaction mixture was allowed to stir at room temperature for 15 min, followed by the addition of 1-bromododecane (48.0 μL, 0.20 mmol). The vial was sealed with a polypropylene cap, removed from the glove box, and was allowed to stir at room temperature for 3 hours. Upon completion, the reaction mixture was diluted with diethyl ether (2 mL), filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 75:1 to 15:1) to isolate the desired product **2.28** (38.6 mg, 93%) and **2.29** (22.4 mg, 50%).



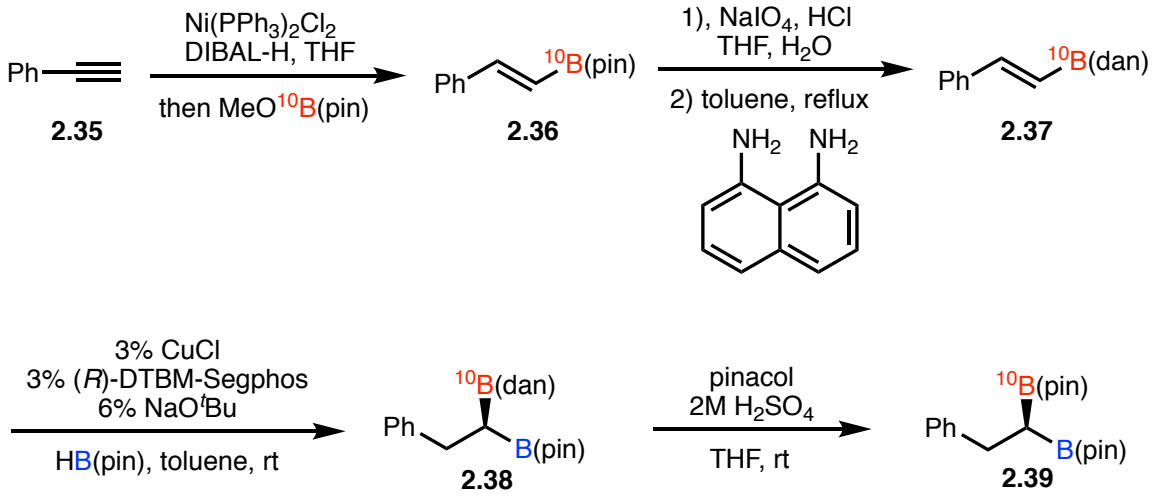
4,4,5,5-tetramethyl-2-(1-phenylpentadecan-3-yl-3-d)-1,3,2-dioxaborolane (2.28). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.25 (2H, m), 7.19-7.14 (3H, m), 2.65-2.54 (2H, m), 1.76-1.70 (1H, m), 1.66-1.60 (1H, m), 1.46-1.34 (2H, m), 1.33-1.21 (32H, m), 0.88 (3H, t, *J* = 6.9 Hz); HRMS-(DART+) for $^{12}C_{27}{}^{1}H_{47}{}^{2}H_{1}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 416.3810, found: 416.3802.



2-(1-(benzyloxy)pentadecan-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.29). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35-7.31 (4H, m), 7.27-7.24 (1H, m), 4.50 (2H, s), 3.44 (2H, t, *J* = 6.8 Hz), 1.79-1.72 (1H, m), 1.70-1.63 (1H, m), 1.44-1.25 (22H, m), 1.20 (12H, s), 1.07-1.02 (1H, m), 0.88 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.8, 128.3, 127.6, 127.3, 82.8, 72.7, 70.0, 31.9, 31.4, 31.3, 29.9, 29.70, 29.66, 29.64, 29.61, 29.57, 29.3, 29.1, 24.8, 24.7, 22.7, 14.1; IR (neat): 2922.3 (s), 2852.4 (s), 1455.0 (w), 1379.7 (m), 1313.9 (m), 1242.6 (w), 1144.7 (s), 1104.0 (m), 967.9 (w), 854.6 (w), 733.7 (m), 696.8 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{28}{}^{1}H_{49}{}^{11}B_{1}{}^{16}O_{3}$ $[M+H]^{+}$: calculated: 445.3853, found: 445.3872.

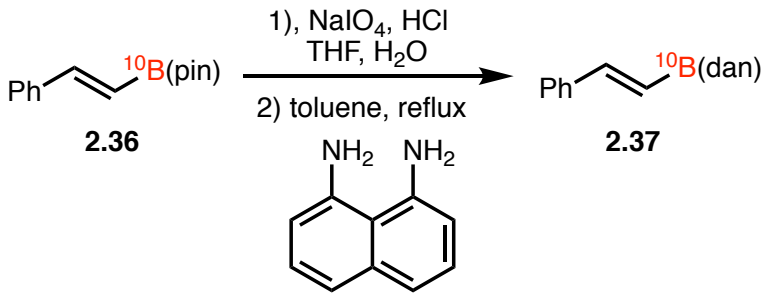
2.5.7 Mass Spectrometry Studies with ^{10}B-labeled Enantioenriched Diboronate Esters

a) Preparation of ^{10}B-labeled Enantioenriched Starting Material:



^{10}B-Labeled-(*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane **2.36** was prepared according to the literature procedure. To an oven-dried 10 mL round-bottom flask with magnetic stir bar was charged with $Ni(PPh_3)_2Cl_2$ (8.2 mg, 12.5 μmol). The flask was sealed with a rubber septum and purged with N_2. THF (2.5 mL) was added *via* syringe, followed by dropwise addition of DIBAL-H (0.49 mL, 2.75 mmol) at room temperature. The resulting black solution was cooled to 0 ^{o}C, and phenylacetylene (0.275 mL, 2.50 mmol) was added dropwise over 5 minutes. The reaction mixture was allowed to warmed to room temperature and stirred for 6 hours. Upon completion, MeO^{10}B(pin)

(786 mg, 5.00 mmol) was added *via* syringe. The reaction mixture was allowed to stir for additional 24 hours, then quenched at 0 °C by dropwise addition of a saturated solution of Rochelle's salt (2.5 mL), then stirred for 1 hour at room temperature. The layers were separated, and the aqueous layer was extracted with diethyl ether (10 mL×3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 25:1 to 10:1) to afford the (*E*)-isomer as a yellow oil in 61% yield (349 mg, 1.52 mmol). The NMR spectra were in accord with previously reported data. HRMS-(DART+) for $^{12}C_{14}{}^{1}H_{20}{}^{10}B_{1}{}^{16}O_2$ $[M+H]^+$: calculated: 230.1593, found: 230.1598.



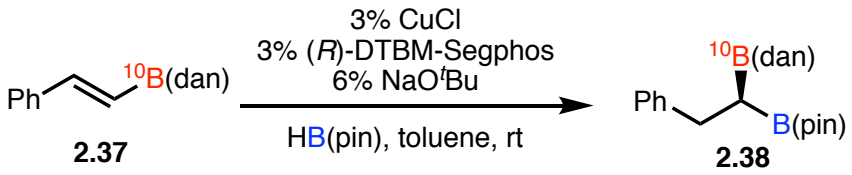
^{10}B-Labeled-(E)-2-styryl-2,3-dihydro-1*H*-naphtho[1,8-*de*][1,3,2]diazaborinine

2.37 was prepared according to the literature procedure with modification.[31] **2.36** (330 mg, 1.43 mmol) and $NaIO_4$ (918 mg, 4.29 mmol) were stirred in a mixture of THF (4 mL)

[31] Koyanagi, M.; Eichenauer, N.; Ihara, H.; Yamamoto, T.; Suginome, M. *Chem. Lett.* **2013**, *42*, 541-543.

and water (1.3 mL) for 30 minutes. Then aqueous HCl was added (1.00 mL, 1.0 M, 1.00 mmol). The reaction was stirred for 17 hours at room temperature. Upon completion, the reaction mixture was diluted with water (3 mL) and extracted with ethyl acetate (6 mL×3). The combined organic layers were washed with water (3 mL×2) and brine (3 mL), dried over Na_2SO_4, filtered, and concentrated.

The unpurified boronic acid and 1,8-diaminonaphthalene (215 mg, 1.36 mmol) were dissolved in toluene (5 mL), equipped with a Dean-Stark apparatus, and heated to reflux for 1.5 h. After cooled to room temperature, the reaction mixture was concentrated in vacuo, and purified on silica gel (hexanes: ethyl acetate = 30:1) to afford **2.37** as a yellow solid (267 mg, 69% yield in two steps). The ^{1}H NMR spectrum was in accord with reported data in literature.[32]



^{10}B-Labeled-2-(2-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-2,3-dihydro-1*H*- naphtho[1,8-*de*][1,3,2]diazaborinine (**2.38**) was prepared according to

[32] Iwadate, N.; Suginome, M. *Org. Lett.* **2009**, *11*, 1899-1902.

the literature procedure.[33] In the glove box, an oven-dried 2-dram vial with magnetic stir bar was charged with CuCl (1.5 mg, 0.015 mmol), NaO*t*-Bu (2.9 mg, 0.030 mmol), (*R*)-DTBM-Segphos (17.7 mg, 0.015 mmol), and toluene (0.4 mL). The mixture was stirred for 10 minutes at room temperature, then pinacolborane (87.0 μL, 0.60 mmol) was added and stirred for an additional 10 minutes. Substrate **2.37** (135.1 mg, 0.50 mmol) in toluene (1.2 mL) was added to the reaction mixture. The reaction was allowed to stir at room temperature for 20 hours. The reaction mixture was filtered through a pad of Celite, washed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes:ethyl acetate = 10:1) to afford **2.38** as a pale grey solid (181 mg, 91% yield, 98:2 er). The ^{1}H NMR spectrum was in accord with reported data in literature.[33]

Analysis of Stereochemistry

The enantioselectivity was determined by SFC analysis of the reaction product. The analogous racemic material was prepared using dppBz as the achiral ligand in the hydroboration reaction. The absolute stereochemistry was assigned according to the literature.

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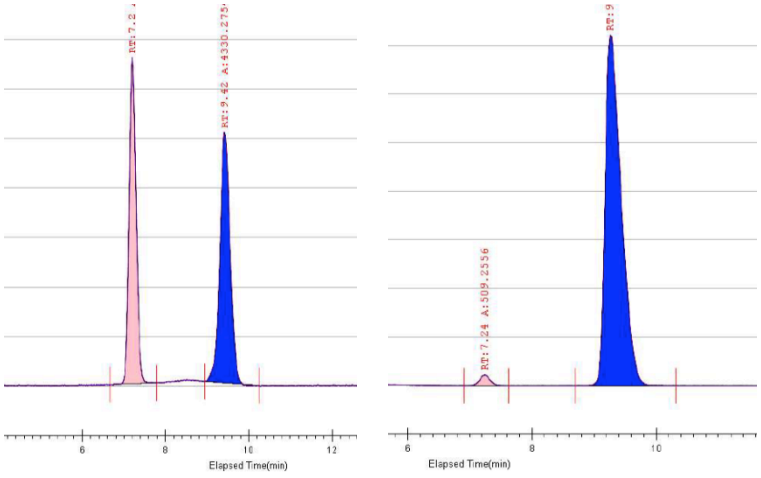
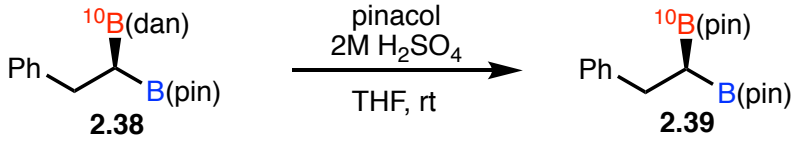
[33] Feng, X.; Jeon, H.; Yun, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 3989-3992.

Chiral SFC (OD-H, Chiraldex, 3 mL/min, 20% i-PrOH, 100 bar, 35 °C)-analysis of the reaction product.



racemic enantioenriched

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	1.929	509.2556	7.24	44.2131	0.0071
2	98.071	25890.7712	9.26	1444.6813	0.0091
Total:	100	26400.0268			



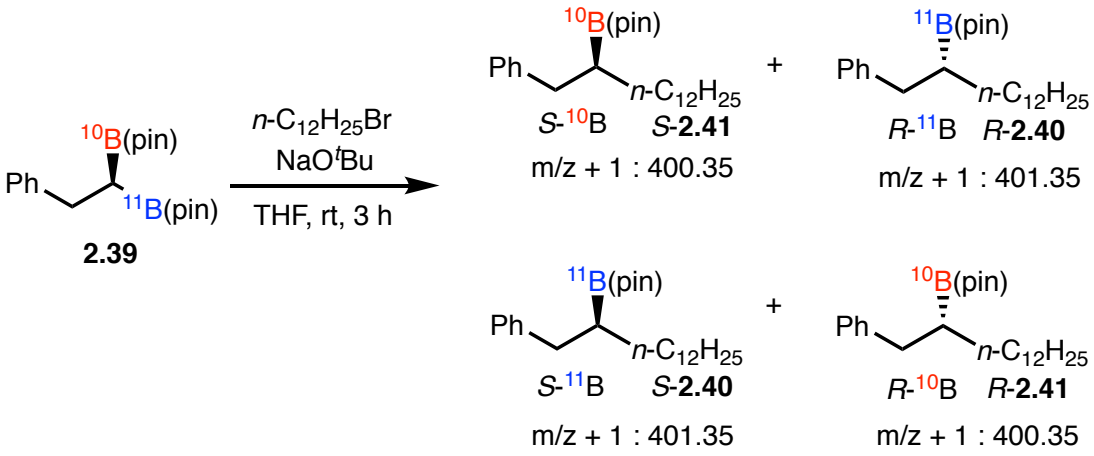
2.38 **2.39**

2.39 was prepared according to the literature procedure.[34] To a stirred solution of **2.38** (143 mg, 0.36 mmol) in THF (3.6 mL) was added aqueous 2 M H_2SO_4 (0.54 mL, 1.08 mmol) and pinacol (213 mg, 1.80 mmol) sequentially. The reaction mixture was stirred at room temperature for 24 hours before quenched by the addition of water (4

[34] Lee, J. C. H.; McDonald, R.; Hall, D. G. *Nature Chemistry*, **2011**, *3*, 894-899.

mL).The reaction mixture was extracted with diethyl ether (3×5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude reaction mixture was purified by chromatography on silica gel (hexanes: diethyl ether = 9:1) to afford the desired product as a colorless oil (103 mg, 80%).

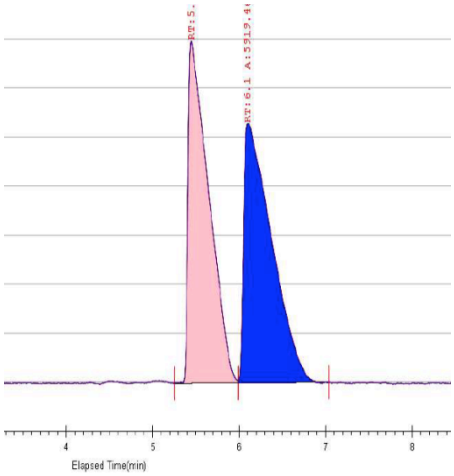
b) Deborylative Alkylation Using ^{10}B-Labeled Enantioenriched Diboronate Ester:



The reaction was performed according to *Representative Procedure for Deborylative Alkylation* with (*S*)-^{10}B-**2.39** (46.4 mg, 0.13 mmol), 1-bromododecane (24.0 μL, 0.10 mmol), NaO*t*-Bu (28.8 mg, 0.30 mmol) and THF (0.50 mL) in 90% yield.

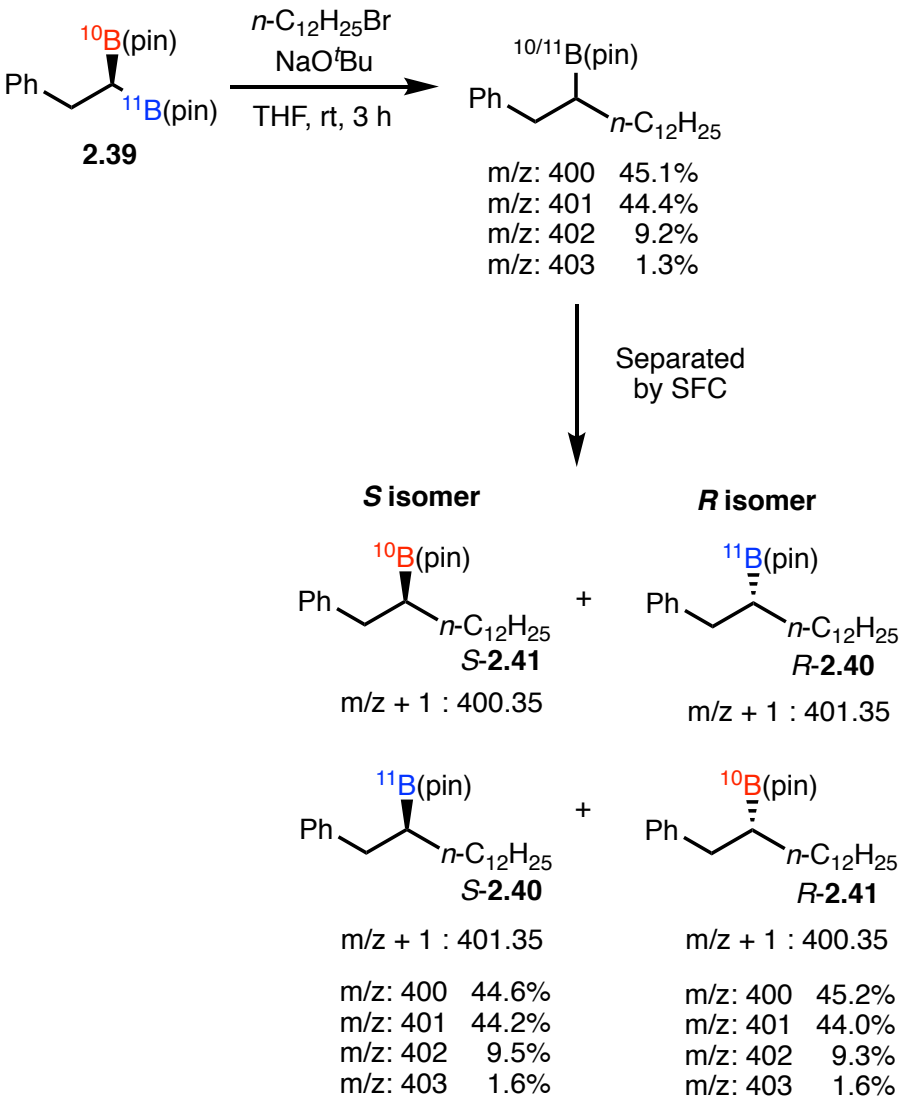
The enantiomers of the product were separated on chiral SFC. Fractions were collected directly from the waste end of SFC instrument (10 seconds for each fraction) and the product (neat) could be easily observed as an oil on the wall of the test tubes. The separated enantiomers were characterized by mass spectrometry.

Chiral SFC (ODR-H, Chiraldex, 3 mL/min, 2% i-PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.



Peak Info					
Peak No	**% Area**	**Area**	**RT (min)**	**Height (mV)**	**K'**
1	49.3381	5764.7867	5.45	348.791	0.0062
2	50.6619	5919.4688	6.1	264.0907	0.0069
Total:	100	11684.2555			

c) Calculation of Mass Spectrometry:



Natural abundance of carbon isotopes is ^{12}C:^{13}C = 0.989:0.011;

Natural abundance of boron isotope is ^{10}B:^{11}B = 0.199:0.801;

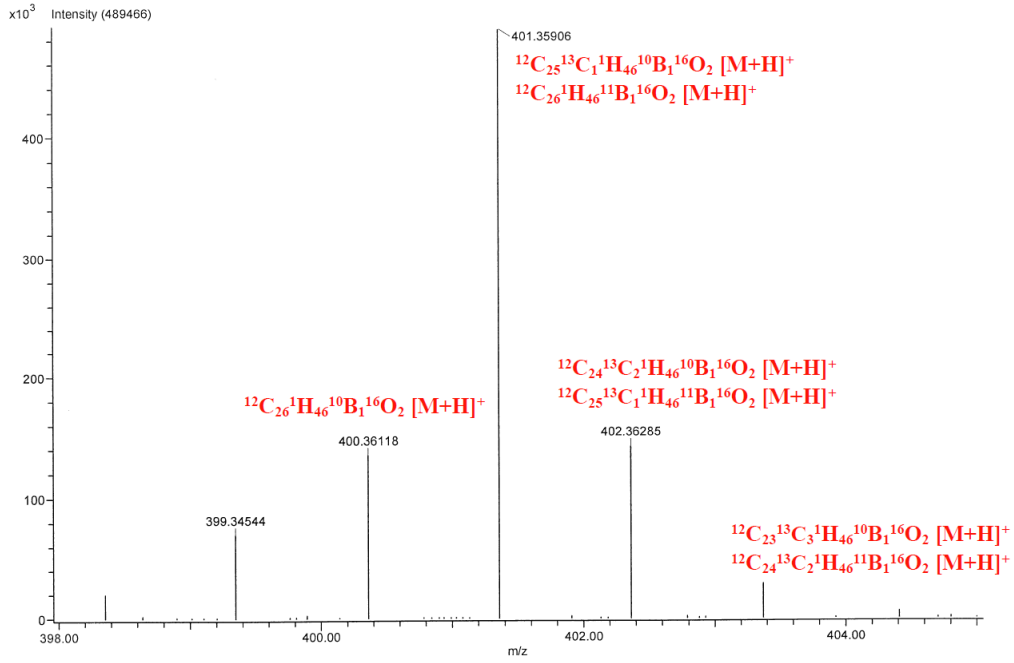
Abundance of boron isotope for the ^{10}B-labeled product is ^{10}B:^{11}B =

(0.500+0.500×19.9%):0.500×80.1% = 0.600:0.400

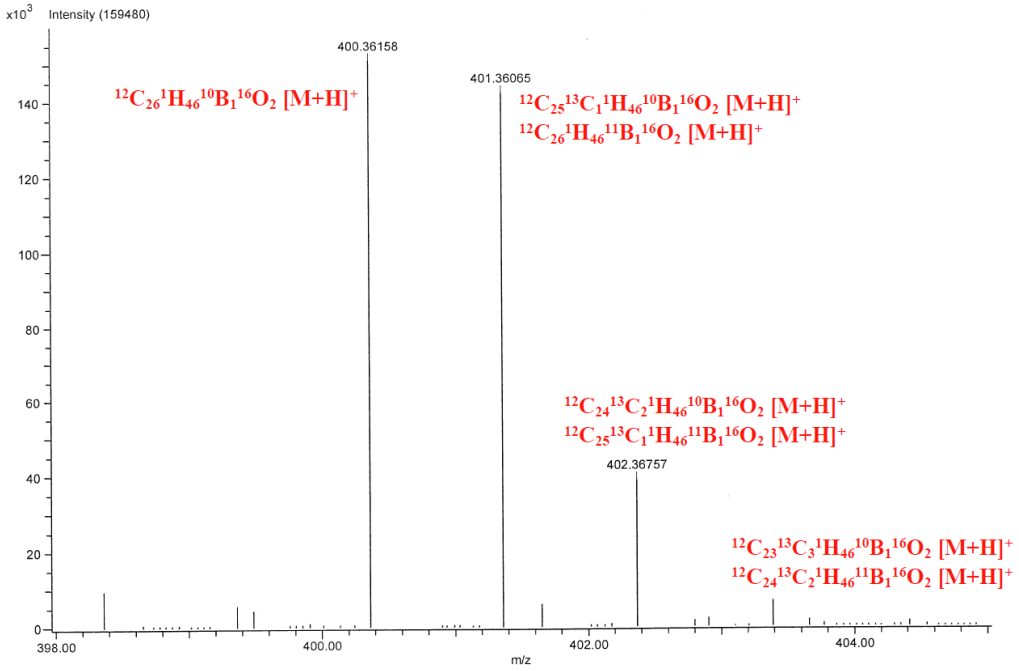
Calculated $[M+H]^+$ distributions for ^{10}B-labeled product:

m/z	Formula of $[M+H]^+$	calculated distribution (assuming racemization)	combined
400	$^{12}C_{26}H_{46}{}^{10}B_1O_2$	$0.989^{26}\times0.600 = 45.0\%$	45.0%
401	$^{12}C_{25}{}^{13}C_1H_{46}{}^{10}B_1O_2$	$(26\times0.989^{25}\times0.011)\times0.600 = 13.0\%$	43.0%
	$^{12}C_{26}H_{46}{}^{11}B_1O_2$	$0.989^{26}\times0.400 = 30.0\%$	
402	$^{12}C_{24}{}^{13}C_2H_{46}{}^{10}B_1O_2$	$(26\times25/2\times0.989^{24}\times 0.011^2)\times0.600 = 1.8\%$	10.5%
	$^{12}C_{25}{}^{13}C_1H_{46}{}^{11}B_1O_2$	$(26\times0.989^{25}\times0.011)\times0.400 = 8.7\%$	
403	$^{12}C_{23}{}^{13}C_3H_{46}{}^{10}B_1O_2$	$(26\times25\times24/3/2\times0.989^{23}\times 0.011^3)\times0.600 = 0.2\%$	1.4%
	$^{12}C_{24}{}^{13}C_2H_{46}{}^{11}B_1O_2$	$(26\times25/2\times0.989^{24}\times 0.011^2)\times0.400 = 1.2\%$	

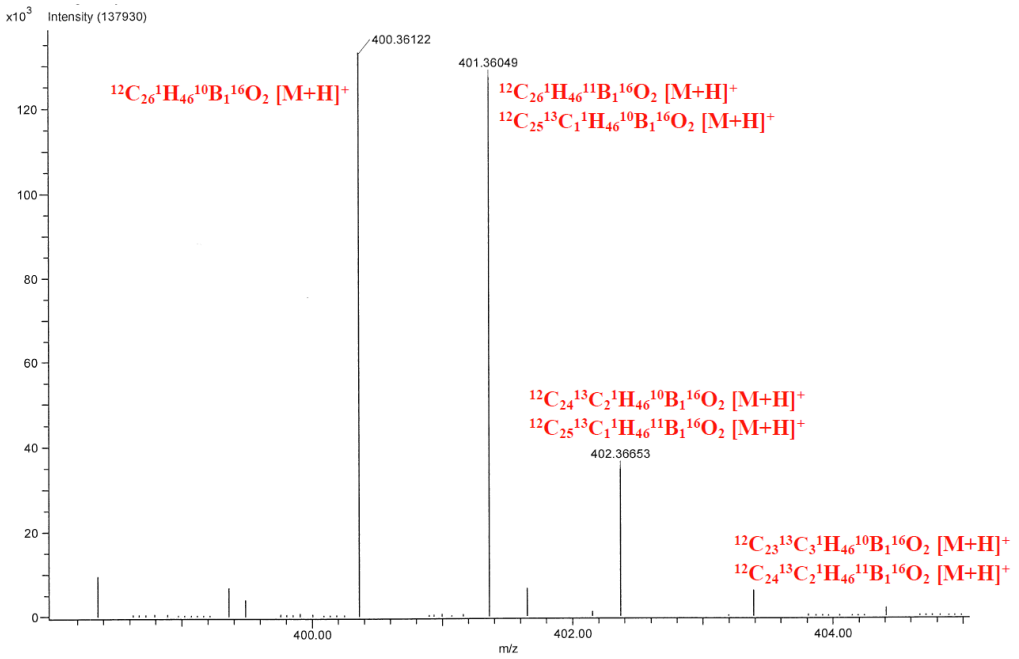
Mass Spectrum of product (±)-2.40 using from non-labeled compound 2.39:



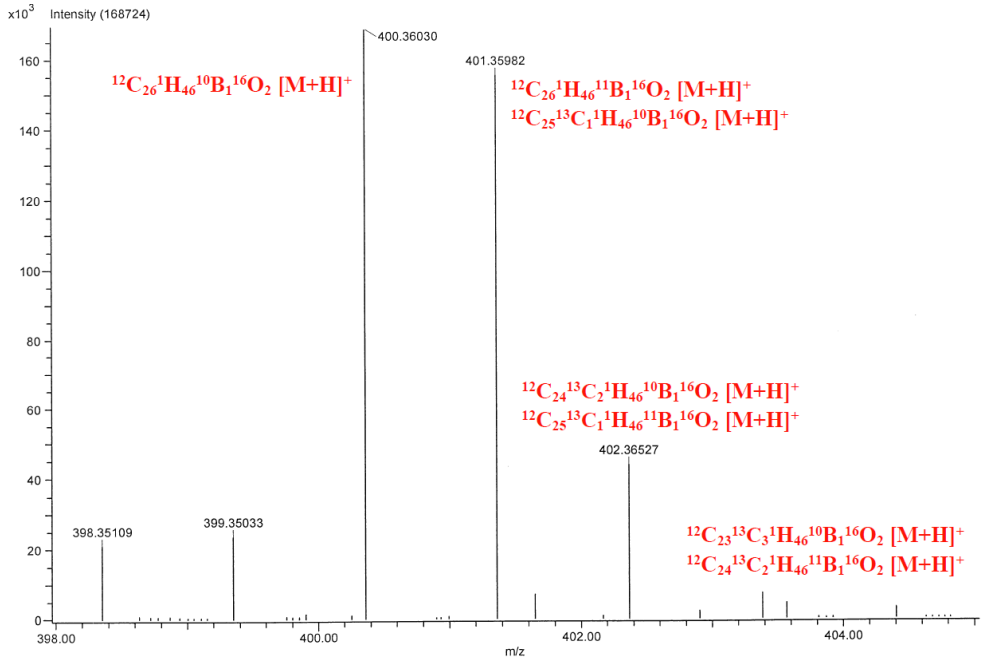
Mass Spectrum of product (±)-2.40 and (±)-2.41 using ^{10}B-labeled compound (S)-^{10}B-2.39:



Mass Spectrum of product (*S*)-2.40 and (*S*)-2.41 from ^{10}B-labeled experiment using (S)-^{10}B-2.39:



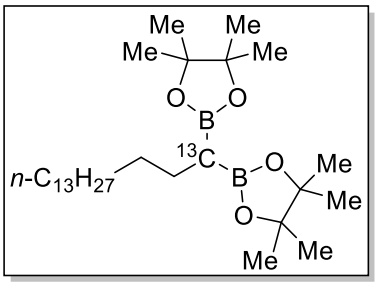
Mass Spectrum of product (*R*)-2.40 and (*R*)-2.41 from ^{10}B-labeled experiment using (S)-^{10}B-2.39:



2.5.8 Analysis of Reaction Intermediates by ^{13}C-Labeled Experiments

a) Preparation of ^{13}C-Labeled *Geminal* Diboronate Ester:

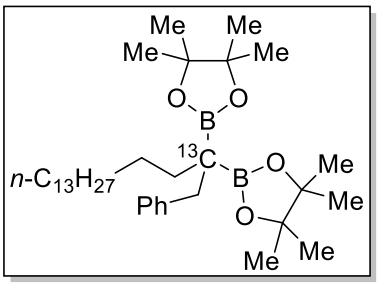
The ^{13}C-labeled diboronate ester **S2.13** was prepared according to *Representative Procedure for Preparation of Geminal Diboronate Esters (Method A)* with CuI (17.3 mg, 0.091 mmol), LiOMe (82.0 mg, 2.16 mmol), $B_2(pin)_2$ (438 mg, 1.73 mmol), 1,1-dibromide (348 mg, 0.91 mmol) and DMF (2 mL). The crude reaction mixture (DMF solution) was directly purified on silica gel (hexanes: diethyl ether = 15:1) to afford the desired product **S2.13** as a colorless oil (261.3 mg, 60%).



2,2'-(1λ^3-hexadecane-1,1-diyl-1-^{13}*C*)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**S2.13**). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.55-1.53 (2H, m), 1.31-1.22 (50H, m), 0.88 (3H, t, *J* = 6.9 Hz), 0.71 (1H, dt, *J* = 111.5, 7.8 Hz). ^{1}H NMR (500 MHz, THF-d_8): δ 1.48 (2H, br s), 1.33-1.27 (26H, m), 1.181 (12H, s), 1.176 (12H, s), 0.89 (3H, t, *J* = 6.9 Hz), 0.56 (1H, dt, *J* = 111.0, 7.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 82.8, 32.6, 31.9, 29.71, 29.70, 29.67, 29.65, 29.62, 29.59, 29.55, 29.4, 25.8, 25.6, 24.8, 24.5, 22.7, 14.1, 10.7 (br, ***C***-B); ^{13}C NMR (125 MHz, THF-d_8): δ 83.4, 33.5, 33.0, 30.87, 30.84, 30.81, 30.79, 30.76, 30.70, 30.5, 26.9, 26.7, 25.4, 25.1, 23.7, 14.6,

11.5 (br, ***C***-B); IR (neat): 2976.9 (w), 2922.5 (s), 2852.9 (m), 1465.8 (w), 1350.5 (m), 1310.3 (s), 1265.4 (m), 1215.0 (w), 1140.2 (s), 969.4 (w), 849.2 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{27}{}^{13}C_1{}^{1}H_{57}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 480.4477, found: 480.4480.

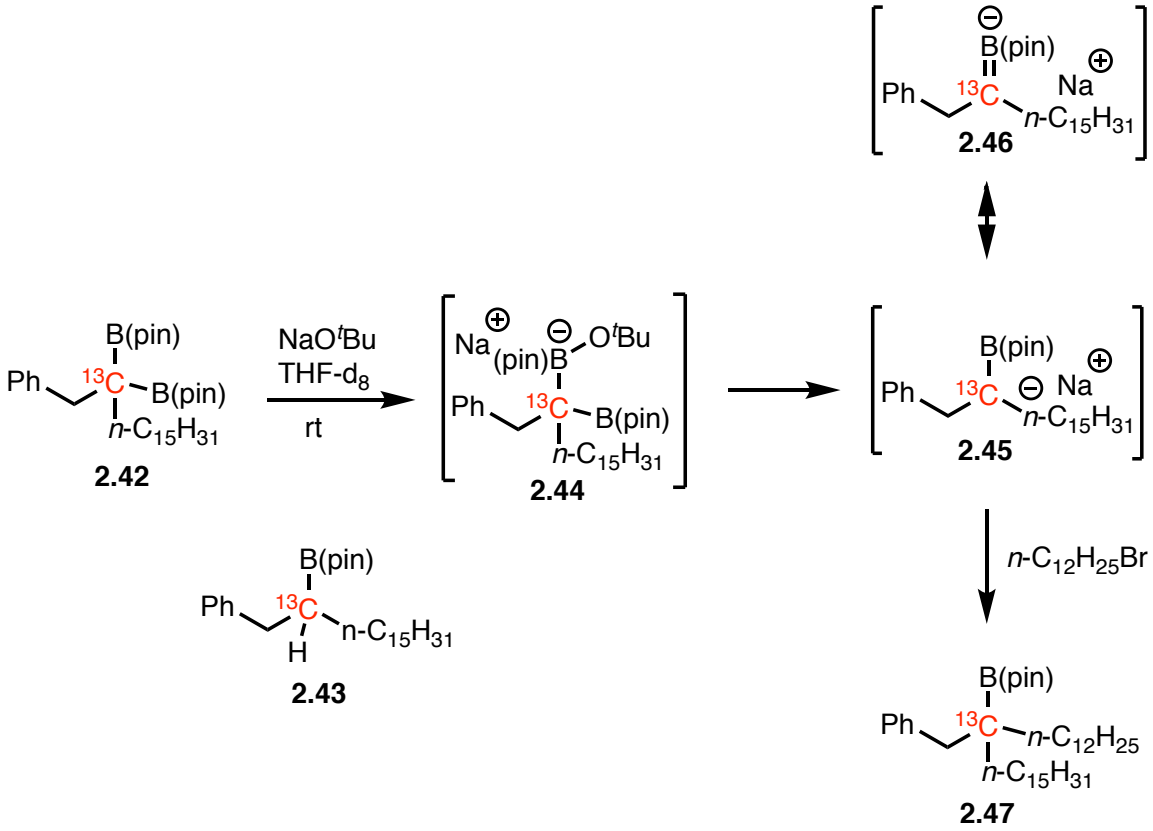
The ^{13}C-labeled diboronate ester **2.42** was prepared according to *Representative Procedure for Preparation of Geminal Diboronate Esters (Method C)* with **S2.13** (118 mg, 0.25 mmol), LTMP (40 mg, 0.27 mmol), benzyl bromide (36 μL, 0.30 mmol) and THF (2.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (20:1 hexanes/diethyl ether, stain in CAM) to afford a colorless oil (95.2 mg, 67%), which turned to a white solid after stored in freezer overnight.



2,2'-(1-phenylheptadecane-2,2-diyl-2-^{13}*C*)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**2.42**). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24-7.18 (4H, m), 7.13-7.10 (1H, m), 2.97 (2H, d, $J_{C\text{-}H}$ = 3.9 Hz), 1.54-1.48 (2H, m), 1.37-1.24 (38H, m), 1.20 (12H, s), 0.88 (3H, t, J = 6.8 Hz); ^{1}H NMR (500 MHz, THF-d_8): δ 7.21-7.20 (2H, m), 7.16-7.13 (2H, m), 7.07-7.04 (1H, m), 2.91 (2H, d, $J_{C\text{-}H}$ = 3.4 Hz), 1.48-1.44 (2H, m), 1.39-1.25 (26H, m), 1.21 (12H, s), 1.17 (12H, s), 0.89 (3H, t, J = 6.9

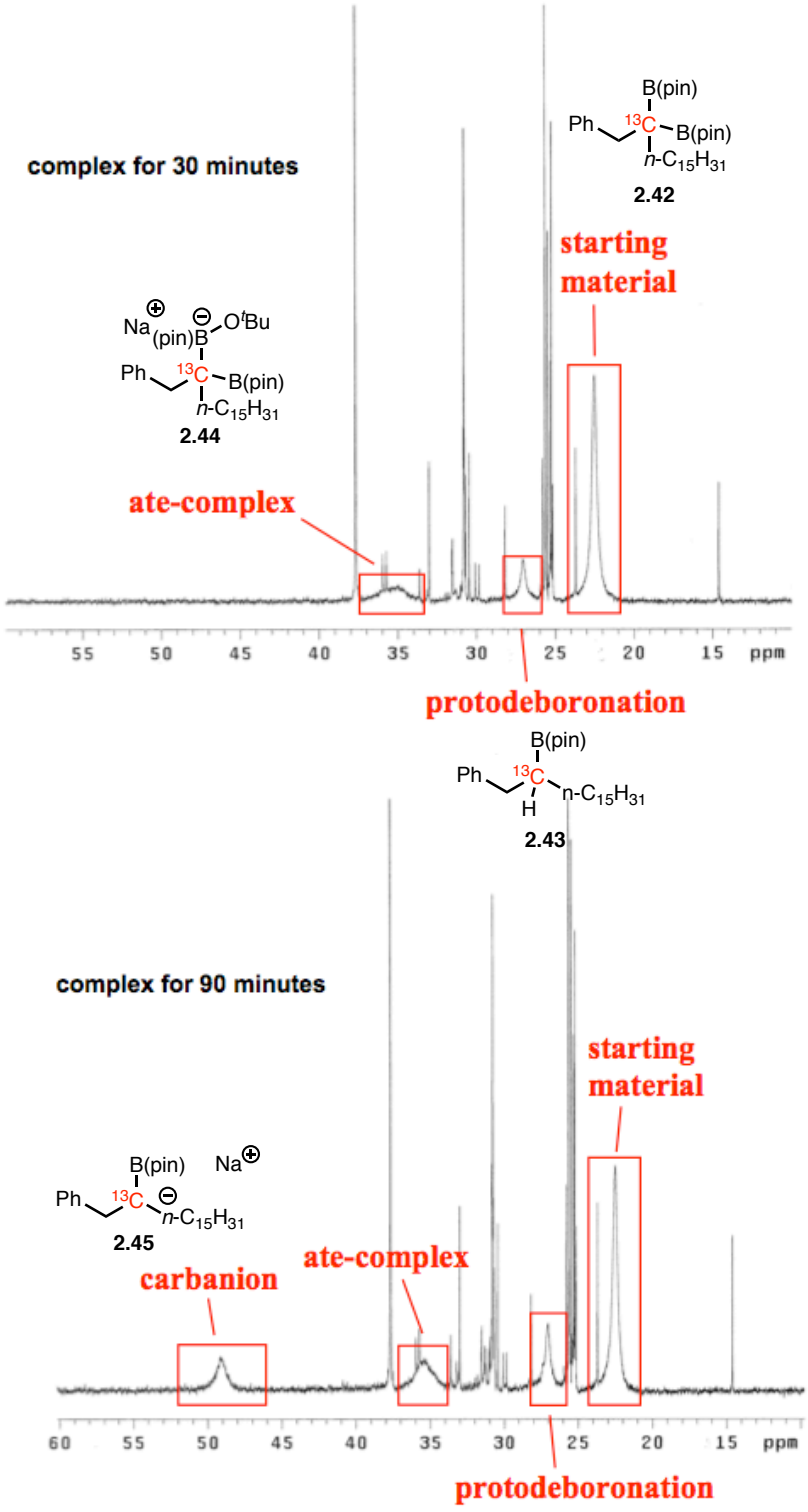
Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.0, 129.7, 127.6, 125.4, 83.1, 34.6, 34.4, 31.9, 30.3, 30.2, 29.71, 29.66, 29.4, 28.8, 28.6, 27.2, 25.0, 24.7, 22.7, 21.6 (br, ***C***-B), 14.1; ^{13}C NMR (125 MHz, THF-d_8): δ 143.2, 130.7, 128.5, 126.3, 83.8, 36.0, 35.8, 33.0, 31.61, 31.57, 30.9, 30.83, 30.79, 30.72, 30.5, 30.1, 29.9, 28.2, 25.7, 25.2, 23.7, 22.6 (br, ***C***-B), 14.6; IR (neat): 2977.9 (w), 2924.1 (s), 2853.4 (m), 1465.4 (w), 1370.9 (m), 1346.6 (m), 1309.8 (m), 1257.4 (m), 1213.1 (w), 1138.8 (s), 972.0 (w), 856.5 (w), 698.7 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{34}{}^{13}C_1{}^{1}H_{63}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: 570.4946, found: 570.4954.

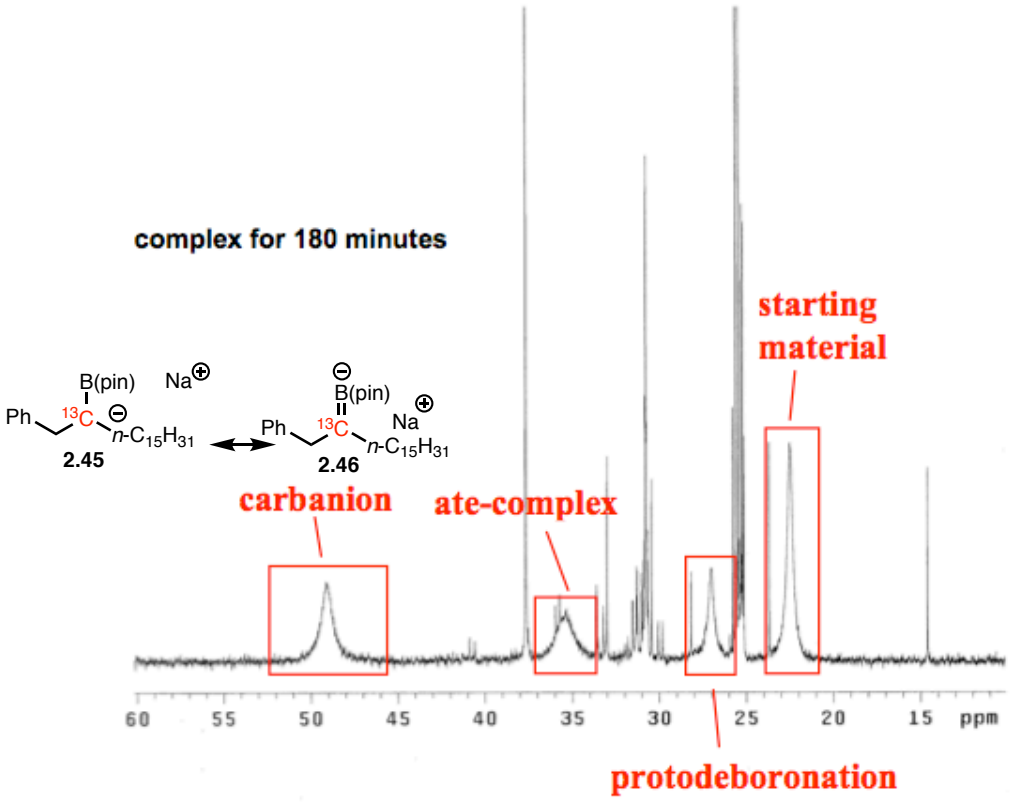
b) ^{13}C NMR Experiments

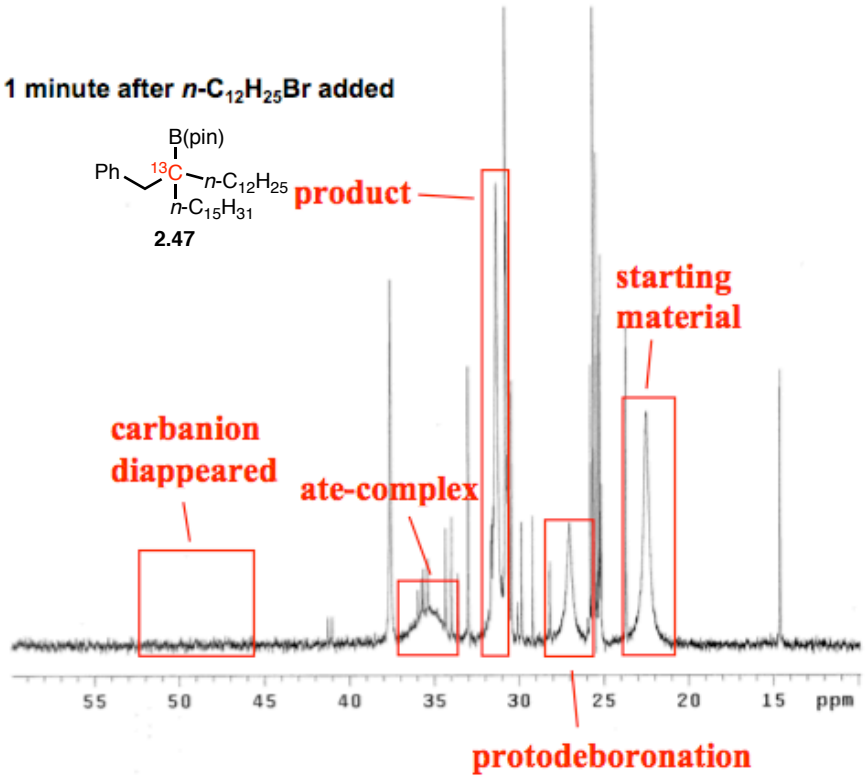


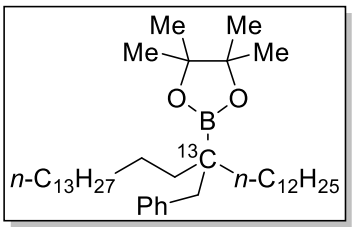
In the glove box, an oven-dried NMR tube was charged with diboronate ester **2.42** (44.4 mg, 0.078 mmol), NaO*t*-Bu (17.3 mg, 0.18 mmol) and THF-d_8 (0.60 mL). The NMR tube was sealed with a rubber septum, removed from the glove box, and monitored by ^{13}C NMR at 25 ^{o}C. After 3 hours, 1-bromododecane (14.4 μL, 0.060 mmol) was added *via* syringe, and the reaction was again tracked by ^{13}C NMR. After 14 hours, the reaction mixture was diluted with diethyl ether, filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 100:1) to afford the desired product **2.47** (24.2 mg, 66% yield) and the protodeboronation product **2.43** (5.3 mg).

^{13}C NMR Spectra of the Reaction (125 MHz, THF-d_8, δ 60–10 ppm):

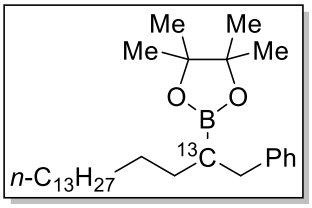

complex for 30 minutes
B(pin)
Ph
13C
B(pin)
n-C15H31
2.42
starting material
Na
(pin)B
OtBu
Ph
13C
B(pin)
n-C15H31
2.44
ate-complex
55 50 45 40 35 30 25 20 15 ppm
protodeboronation
B(pin)
Ph
13C
n-C15H31
H
2.43
complex for 90 minutes
starting material
B(pin)
Na
Ph
13C
n-C15H31
2.45
carbanion
ate-complex
60 55 50 45 40 35 30 25 20 15 ppm
protodeboronation


complex for 180 minutes
B(pin)
Na
Ph
13C
n-C15H31
2.45
B(pin)
Ph
13C
Na
n-C15H31
2.46
carbanion
ate-complex
starting material
protodeboronation
60
55
50
45
40
35
30
25
20
15
ppm


1 minute after n-C12H25Br added
B(pin)
Ph
13C
n-C12H25
n-C15H31
2.47
product
starting material
carbanion diappeared
ate-complex
protodeboronation
55
50
45
40
35
30
25
20
15
ppm

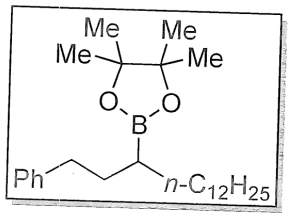


2-(13-benzyloctacosan-13-yl-13-^{13}C)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2.47**). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24-7.21 (2H, m), 7.18-7.13 (3H, m), 2.70 (2H, d, $J_{C\text{-}H}$ = 4.4 Hz), 1.29-1.27 (50H, m), 1.21 (12H, s), 0.89 (6H, t, J = 7.3 Hz); ^{1}H NMR (500 MHz, THF-d_8): δ 7.17-7.16 (4H, m), 7.11-7.07 (1H, m), 2.67 (2H, d, $J_{C\text{-}H}$ = 3.9 Hz), 1.36-1.30 (50H, m), 1.20 (12H, s), 0.89 (6H, t, J = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.2, 130.3, 127.6, 125.5, 83.0, 40.0, 39.7, 34.4, 34.2, 31.9, 30.5, 30.4, 30.3 (br, ***C***-B), 29.72, 29.69, 29.67, 29.4, 25.1, 24.8, 22.7, 14.1; ^{13}C NMR (125 MHz, THF-d_8): δ 141.3, 141.2, 131.21, 131.20, 128.5, 126.5, 83.96, 83.95, 41.3, 41.0, 35.7, 35.4, 33.0, 31.69, 31.65, 31.4 (br, ***C***-B), 30.84, 30.83, 30.82, 30.79, 30.78, 30.76, 30.5, 26.0, 25.6, 23.7, 14.6; IR (neat): 2921.2 (s), 2851.7 (m), 1463.9 (m), 1376.8 (m), 1307.3 (m), 1264.9 (w), 1211.6 (w), 1143.5 (m), 966.3 (w), 854.1 (w), 721.6 (w), 701.3 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{40}{}^{13}C_1{}^{1}H_{76}{}^{11}B_1{}^{16}O_2$ $[M+H]^+$: calculated: 612.5972, found: 612.5984.

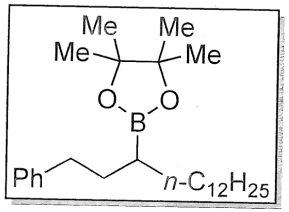


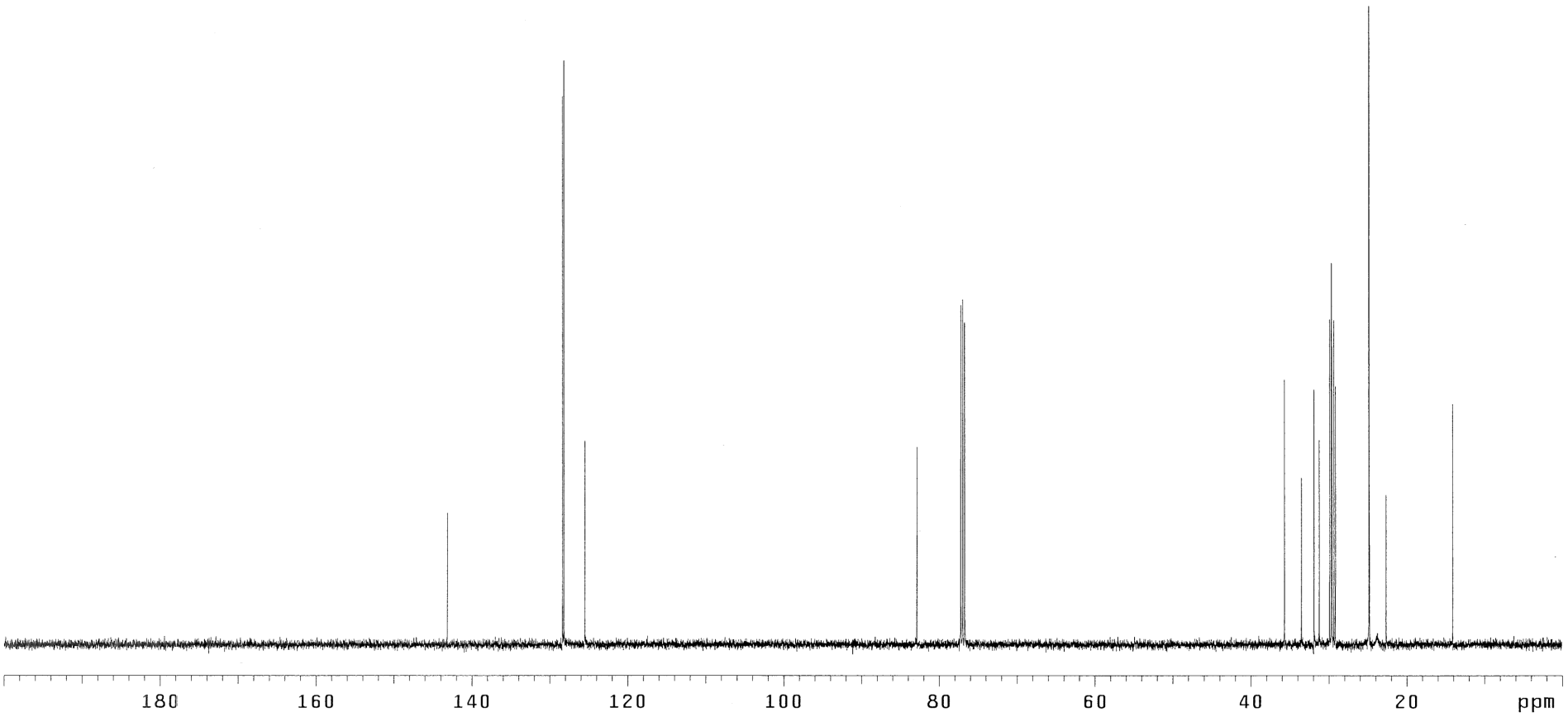
2-(13-benzyloctacosan-13-yl-13-^{13}C)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2.43**). ^{1}H NMR (500 MHz, THF-d_8): δ 7.19-7.14 (4H, m), 7.09-7.05 (1H, m), 2.72-2.66 (1H, m), 2.61-2.56 (1H, m), 1.42-1.29 (28H, m), 1.20-1.14 (1H, m), 1.14 (6H, s), 1.11 (6H, s),

0.89 (3H, t, J = 7.3 Hz); ^{13}C NMR (125 MHz, THF-d_8): δ 143.6, 129.8, 128.8, 126.4, 83.7, 38.5, 38.3, 33.0, 32.3, 32.1, 31.01, 30.98, 30.81, 30.77, 30.7, 30.5, 30.1, 27.1 (br, ***C***-B), 25.5, 25.32, 25.28, 23.7, 14.6; IR (neat): 2921.9 (s), 2852.2 (m), 1455.8 (w), 1371.2 (m), 1317.3 (m), 1143.8 (m), 967.3 (w), 862.4 (w), 743.1 (w), 698.3 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{28}{}^{13}C_1{}^{1}H_{52}{}^{11}B_1{}^{16}O_2$ $[M+H]^+$: calculated: 444.4094, found: 444.4094.


Me
Me
Me
Me
O
O
B
Ph
n-C12H25

9
8
7
6
5
4
3
2
1
ppm


Me
Me
Me
Me
O
O
B
Ph
n-C12H25


180
160
140
120
100
80
60
40
20
ppm

Chapter 3

Development of A Boron Alkylidene-Alkene Cycloaddition Reaction

3.1 Introduction

For the deborylative alkylation of geminal bis(boronate) esters, it was proposed that a boron stabilized carbanion, rather than a radical is the reactive intermediate based on mechanistic studies.[56] For example, in the presence of an alkene, the desired base-promoted deborylative alkylated product (**2.16**) was obtained in 91% yield (Scheme 3.1) with no cyclized product observed. However, not fully convinced of the anion pathway, it was considered that the radical pathway could also operate for this transformation. To gain further insight for this hypothesis, a deborylative alkylation reaction of 1,1-diboryl-alkane **3.1** in the absence of electrophile was performed. Upon quenching the reaction with diethyl ether and purification with silica gel column chromatography, the cyclized five-membered ring product (**3.2**) was obtained in high diastereoselectivity (13:1 dr), but relatively low yield (13%) (Scheme 3.2).

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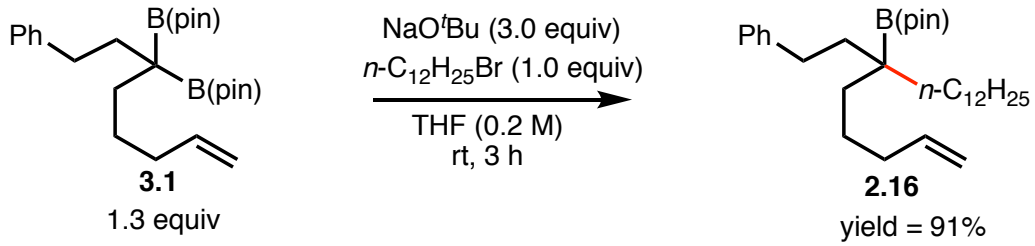
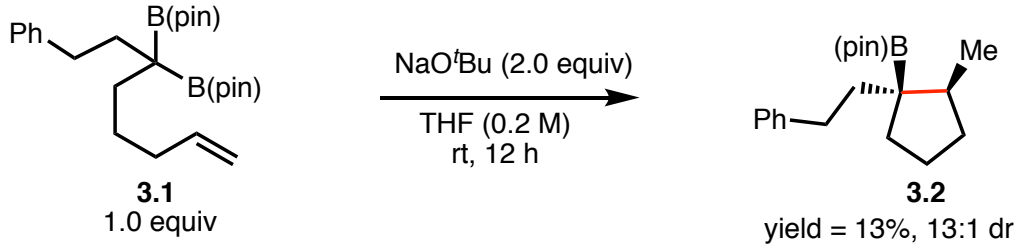
[56] Hong, K.; Liu, X.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 10581-10584.

Scheme 3.1 Deborylative Alkylation Reaction of Geminal Bis(boronic) Ester with An Electrophile



Scheme 3.2 Deborylative Alkylation Reaction of Geminal Bis(boronic) Ester without An Electrophile



Alkyl boronic esters are of great synthetic value as they can be easily converted into a wide array of functional groups such as amines,[57] alkynes,[58] ketones,[59] homologated boronic esters,[60] alcohols,[61] carboxylic acids,[62] alkenes[63] and allylic

---

[57] Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449-16451.

[58] Wang, Y.; Noble, A.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2016**, 55, 4270-4274.

[59] Pulis, A. P.; Blair, D. J.; Torres, E.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2013**, *135*, 16054-16057.

[60] (a) Sadhu, K. M.; Matteson, D. S. *Organometallics* **1985**, *4*, 1687-1689. (b) Matteson, D. S. *J. Org. Chem.* **2013**, *78*, 10009-10023. (e) Matteson, D. S. *Chem. Rev.* **1989**, *89*, 1535-1551.

[61] Brown, H. C.; Snyder, C.; Subba Rao, B. C.; Zweifel, G. *Tetrahedron* **1986**, *42*, 5505-5510.

[62] Chen, A. C.; Ren, L.; Crudden, C. M. *J. Org. Chem.* **1999**, *64*, 9704-9710.

[63] Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652-3653.

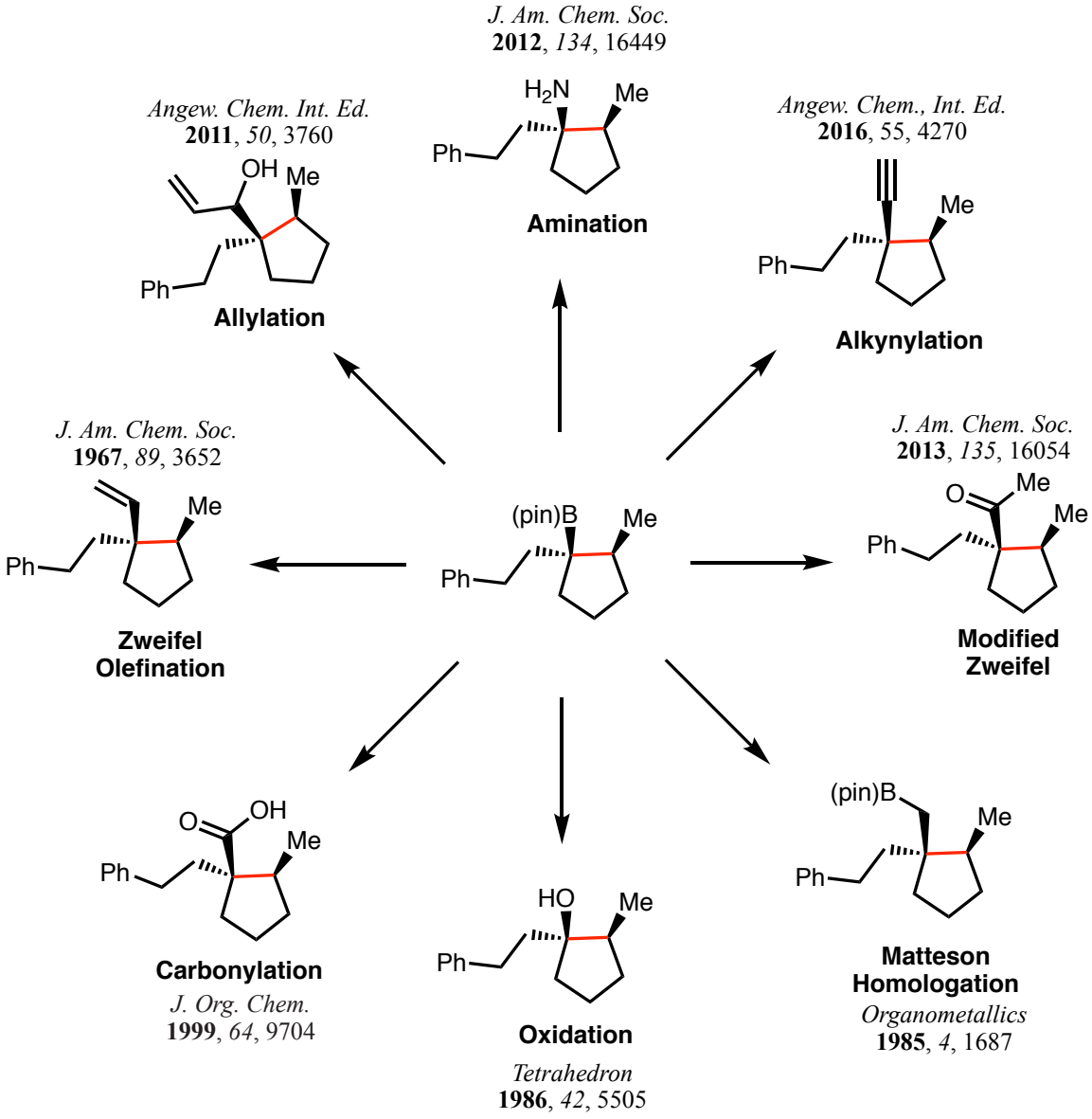
alcohols[64] (Scheme 3.3). Also, five-membered rings are prevalent in natural products[65] (Shown in Scheme 3.4). Based on these facts, we considered that the development of this deborylative cyclization method would be meaningful and synthetically useful.

---

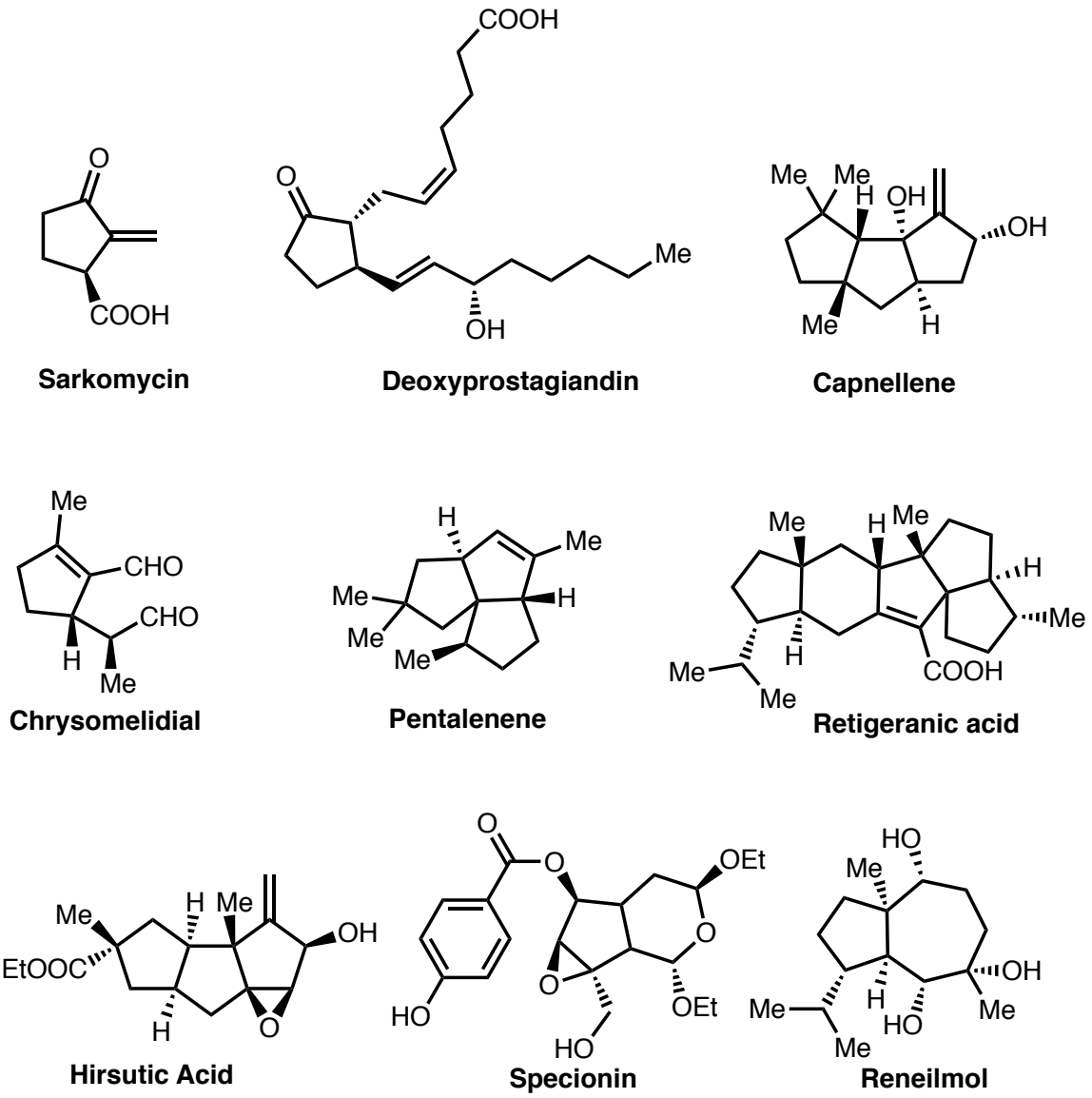
[64] Sonawane, R. P.; Jheengut, V.; Rabalakos, C.; Larouche-Gauthier, R.; Scott, H. K.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2011**, *50*, 3760-3763.

[65] (a) Hudlicky, T.; Price, J. D. *Chem. Rev.* **1989**, *89*, 1467-1486. (b) Ai, Y.; Kozytska, M. V.; Zou, Y.; Khartulyari, A. S.; Smith, A. B., III *J. Am. Chem. Soc.* **2015**, *137*, 15426-15429. (c) Yahata, K.; Ye. N.; Iso. K.; Ai, Y.; Lee. J.; Kishi. Y. *J. Org. Chem*. **2017**, *87,* 8808-8830. (d) Yahata, K.; Ye, N.; **Ai, Y**.; Iso. K.; Kishi, Y. *Angew. Chem. Int. Ed*. **2017**, *56*, 10796-10800.

Scheme 3.3 Different Transformations of Alkyl Boronic Esters



Scheme 3.4 Selected Natural Products Containing Five-Membered Rings



3.2 Background

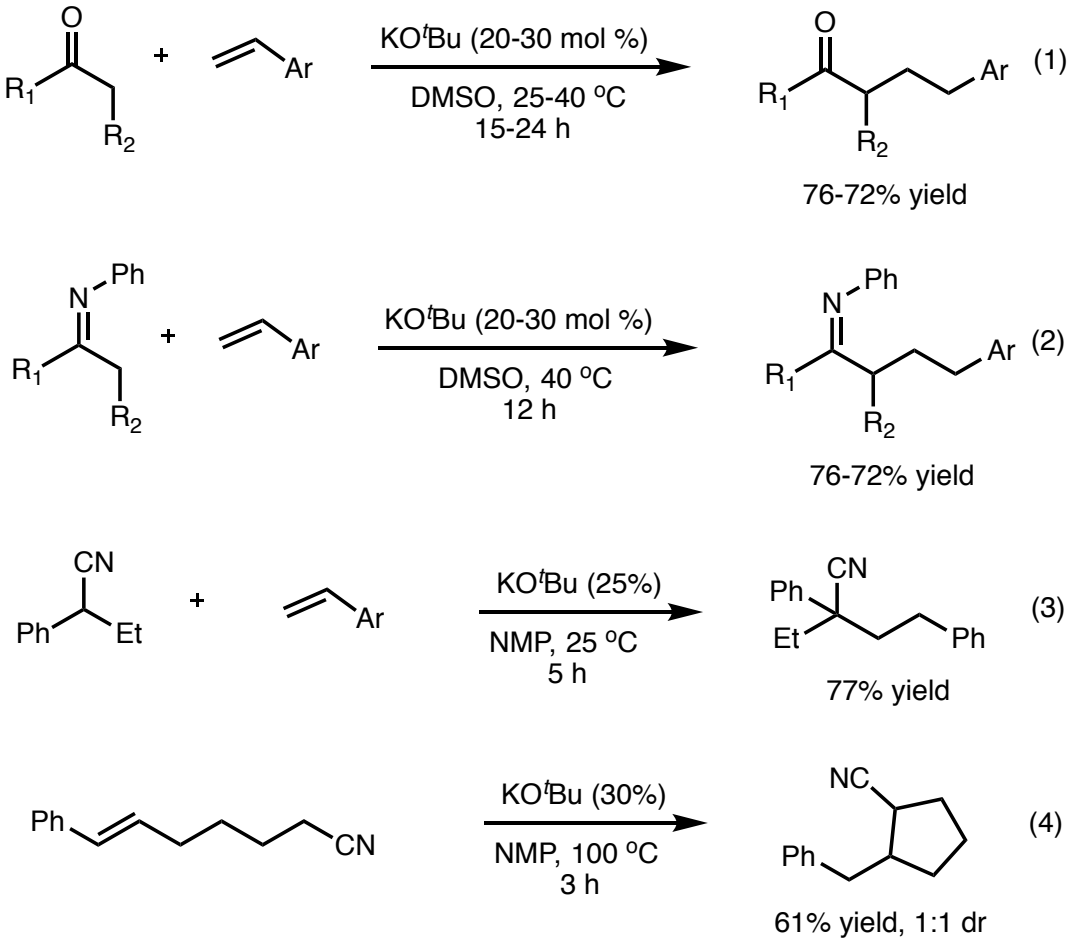
There were few reports of a stabilized carbanion adding to an unactivated alkene in the literature. Knochel and coworkers demonstrated one of the few examples (Scheme

3.5).[66] They revealed that in the presence of a catalytic amount of KO^{t}Bu, ketones, imines and nitriles could add to styrenes intermolecularly to afford the addition products in good yield (Scheme 3.5, equation 1-3). Notably, they also obtained cyclized products (Scheme 3.5, equation 4) in moderate yield but poor diastereoselectivity with catalytic amount of KO^{t}Bu. Considering the substrates and the reaction conditions, this transformation was not likely to involve the intermediacy of radicals and likely benefits from the effective participation of the styrene. Of note, 2,6-di-*tert*-butyl-4-methylphenol did not inhibit the reaction, which was further evidence to rule out the possibility of radical intermediates.

---

[66] Rodriguez, A. L.; Bulaksananusorn, T.; Knochel, P. *Org. Lett.* **2000**, *2*, 3285-3287.

Scheme 3.5 Stabilized Carbanion Adding to Unactivated Alkenes

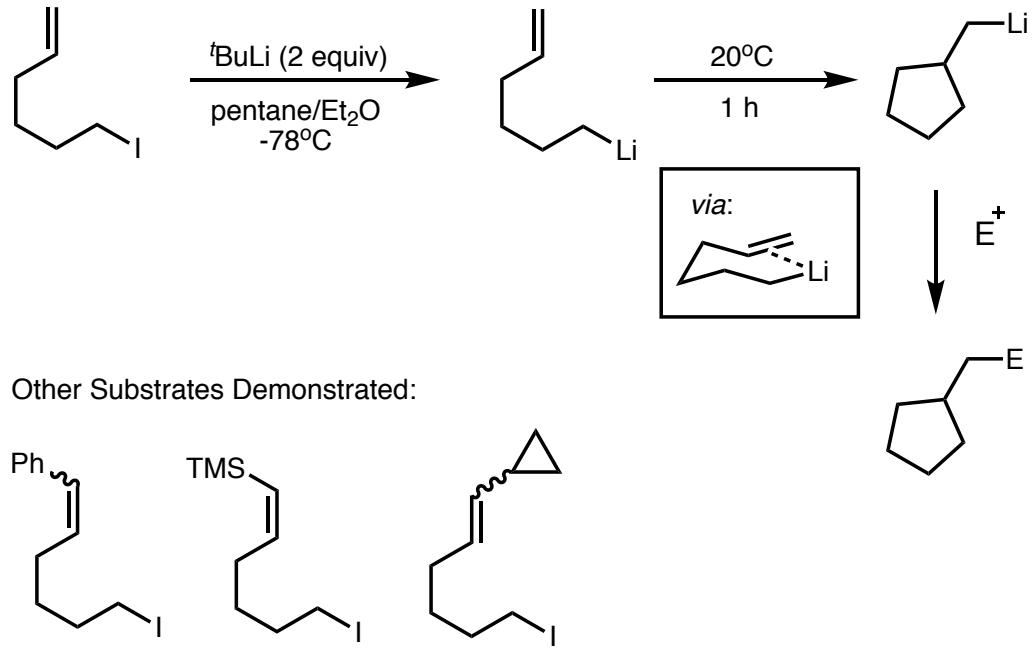


Bailey and coworkers[67] illustrated that 5-hexenyllithium cyclizes on itself. They noted hydrogen, phenyl, trimethylsilyl and cyclopropyl substituents are tolerated to furnish five-membered ring products through 5-*exo* cyclization, which positions lithium at the primary carbon position (Scheme 3.6). This alkyl lithium intermediate could further

[67] (a) Bailey, W. F.; Khanolkar, A. D.; Gavaskar, K.; Ovaska, T. V.; Rossi, K.; Thiel, Y.; Wiberg, K. B. *J. Am. Chem. Soc.* **1991,** *113*, 5720-5727. (b) Bailey, W. F.; Gavaskar, K. V. *Tetrahedron* **1994,** *50*, 5957-5970.

be trapped by a variety of electrophiles, leading to cyclized products containing diversified functionalities such alcohols and carboxylic acids.

Scheme 3.6 Cyclization of Unsaturated Alkyllithium

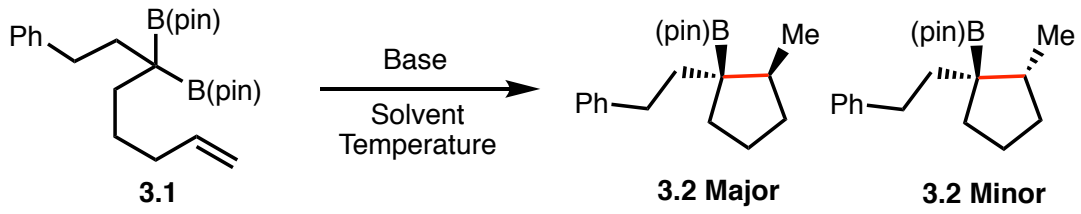


3.3 Development of Deborylative Cyclization of Olefinic Geminal Bis(boronates)

3.3.1 Screening for Optimal Reaction Condition

Even though we were deeply intrigued by the mechanism behind this boron alkylidene-alkene cycloaddition, we first decided to optimize the reaction conditions. After screening bases, we found KO^{t}Bu offered the highest reactivity, while NaO^{t}Bu provided us the highest diastereoselectivity (Table 3.1, Entry 1 vs Entry 7). For optimal solvents, even though toluene afforded better reactivity (Entry 9), THF delivered the best balance between reactivity and selectivity (Entry 7). Thus, the combination of KO^{t}Bu and THF was applied in further substrate scope investigations and mechanistic studies.[68]

Table 3.1 Optimization of Deborylative Cyclization of 1,1-Diboryl Alkenes



3.1 **3.2 Major** **3.2 Minor**

[68] Liu, X.; Deaton, T. M.; Haeffner, F.; Morken, J. P. *Angew. Chem., Int. Ed.* **2017**, *56*, 11485-11489.

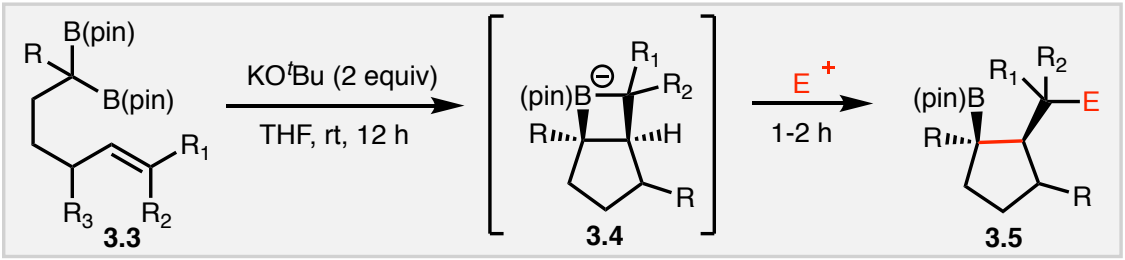
entry	base	solvent	yield (%)	d.r. (3.2 major : 3.2 minor)
1	NaO*t*-Bu	THF	12	13 : 1
2	NaO*t*-Bu	toluene	<5	N/A
3	KOMe	toluene	<5	N/A
4	KO*t*-Bu	DCE	<5	N/A
5	KO*t*-Bu	hexanes	39	2.2 : 1
6	KO*t*-Bu	THF	51	5 : 1 [b]
7	KO*t*-Bu	THF	52	4 : 1
8	KO*t*-Bu	toluene	52	2 : 1 [b]
9	KO*t*-Bu	toluene	61	1.2 : 1

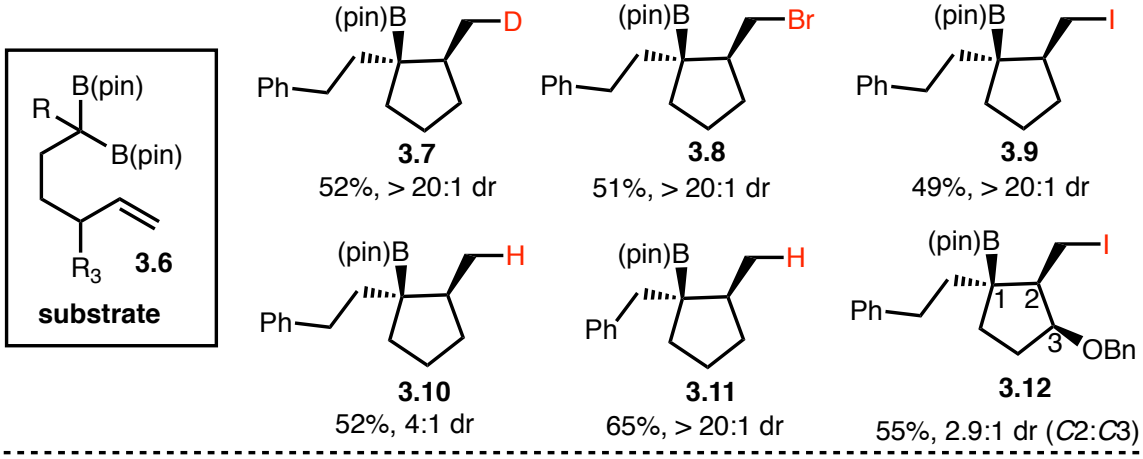
[a] Reaction conditions: 1,1-diboronate ester (0.10 mmol, 0.2 M), base (0.20 mmol), and room temperature. Yield refers to the isolated yield of purified material. Diastereoselectivity was determined based on NMR integration. [b] Reaction conducted at 50 °C.

3.3.2 Substrate Scope for Deborylative Cyclization Reaction

With the optimized deborylative cyclization reaction conditions in hand, we probed different substrates to learn more about the scope of the reaction. For geminal bis(boronate) esters containing terminal alkenes such as **3.6**, the alkylidene-alkene cycloaddition occured very efficiently affording the desired product **3.5** in good yield. H_2O, D_2O, NBS and I_2 were very good electrophiles, delivering the desired cyclized products **3.10**, **3.7**, **3.8**, and **3.9,** respectively, in good yield and diastereoselectivity. A coordinating oxygen atom did not interfere with this transformation, affording cyclized product **3.12** in 55% yield.

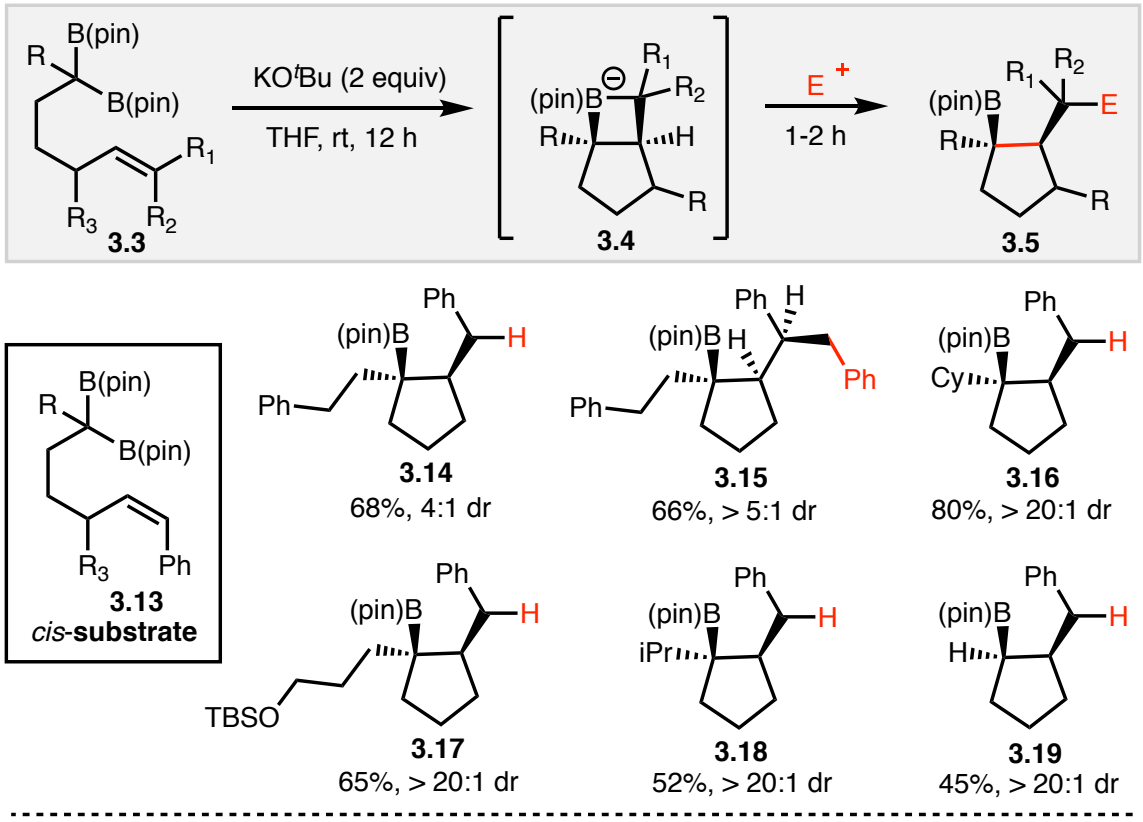
Scheme 3.3 Substrate Scope for Mono-substituted Alkenes





This boron alkylidene-alkene cycloaddition methodology does not only work well for monosubstituted alkenes, but also works well for 1,2-disubstituted *cis*-styrene derivatives such as **3.13**. For electrophiles, they can be as simple as proton to deliver cyclized product **3.14**, or as bulky as benzyl bromide to give product **3.15**. The R substituent in compound **3.3** seems to have little effects on the result; they can range from sterically hindered cyclohexyl **3.16** to silyl protected alcohol **3.17**, and to simple proton **3.19**. All substrates provided cyclized products in good yield and synthetically useful diastereoselectivity.

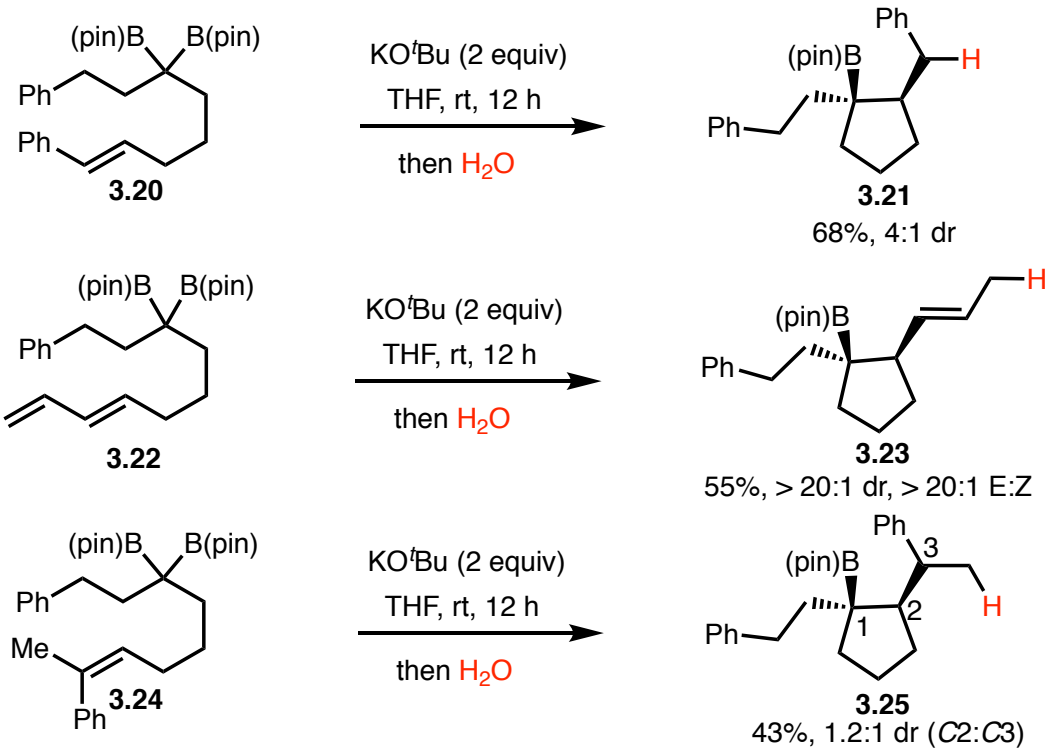
Scheme 3.4 Substrate Scope for *cis*-Styrene Type Alkenes



With the good performance of *cis*-styrene derivatives in this system, we were curious about how *trans*-styrenes would behave. *Tetra*-substituted-1,1-diborylalkane **3.20** was synthesized and treated with the standard reaction conditions. Surprisingly, *trans*-substrate **3.20** performed equally well as the *cis*-styrene **3.13** (68% yield, 4:1 dr) to give the same diastereomer in similar yield and diastereoselectivity. The mono-substituted alkene could also be extended to conjugated 1,3-diene **3.22**, which furnished the ring cyclized product **3.23** in good yield (55%) and excellent selectivity (> 20:1 dr). For *tri*-substituted alkene **3.24**, the yield was diminished, as well as the diastereoselectivity. We hypothesized that the steric difference between methyl and

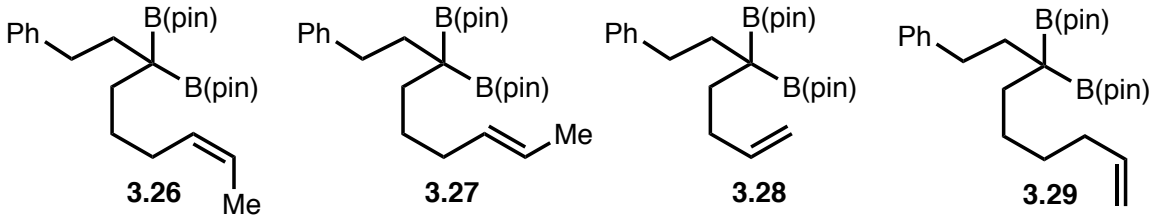
phenyl group was not big enough to induce a large enough bias for a high diastereoselectivity.

Scheme 3.5 Substrate Scope for Other Type Alkenes



While we obtained a wide array of products in good yield and diastereoselectivity, not all substrates were well behaved. Some substrates did not afford the desired products, namely, with 1,2-disubstituted aliphatic alkenes, neither *cis* nor *trans* (**3.26** and **3.27**) underwent cylization. Substrates **3.28** or **3.29** did not deliver the four-membered ring or six-membered ring products respectively. The substrates in Scheme 3.6 usually led to protodeborylation byproducts.

Scheme 3.6 Alkenes Did Not Yield the Expected Products

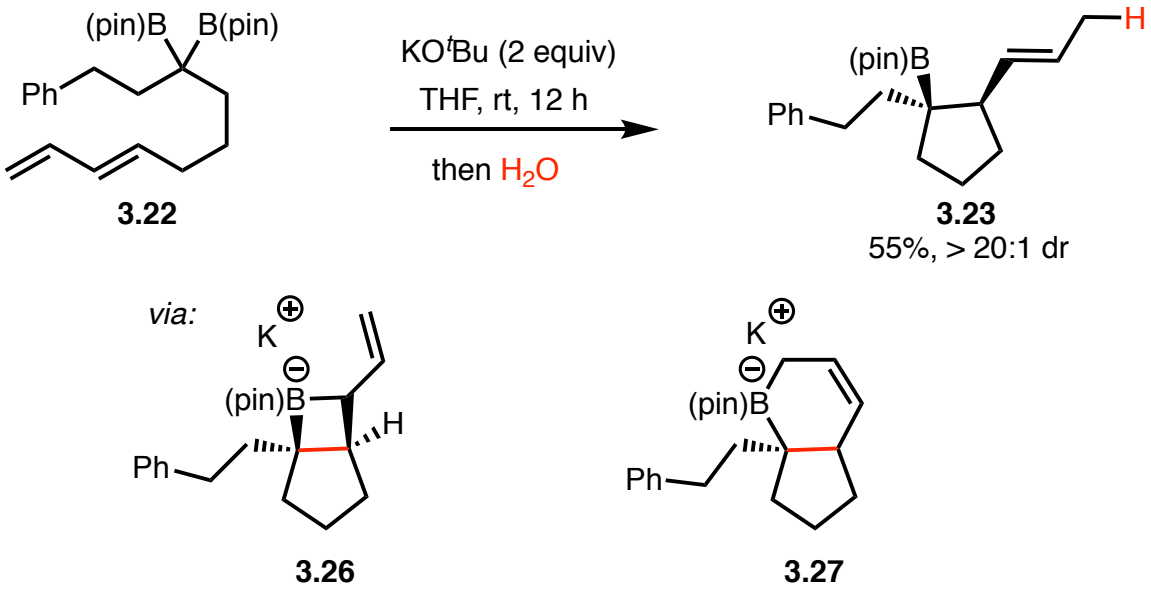


3.4 Mechanistic Studies

3.4.1 Evidence for a Four-Membered Ring Intermediate

Because 1,3-diene substrate **3.22** delivered the cyclized product with the *trans*-alkene geometry, we proposed a four-membered ring intermediate **3.26** instead of six-membered ring intermediate **3.27**, based on this stereochemical outcome. We attempted to grow crystals of this four membered-ring intermediate, however, were never successful even after many attempts. ^{13}C NMR spectroscopy was put forward to confirm the existence of this intermediate.

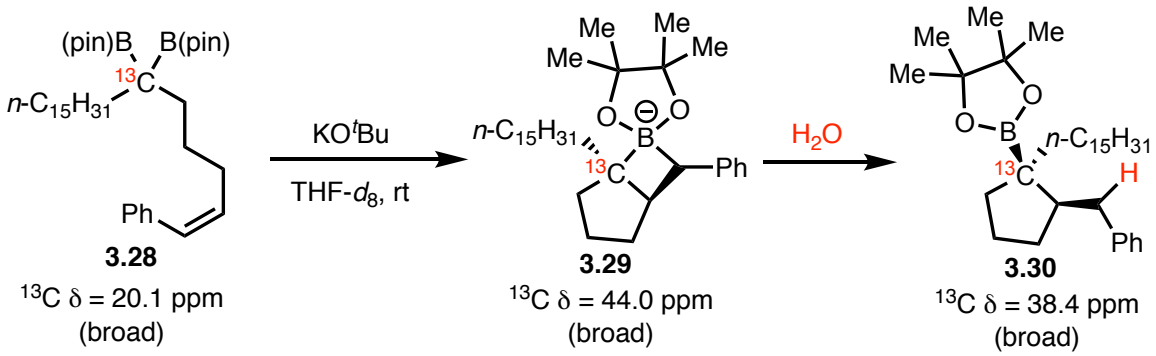
Scheme 3.8 Proposed Four-membered Ring Intermediate



^{13}C labeled geminal bis(boronic) ester **3.28** was synthesized. It was treated with KO^{t}Bu in d_8-THF and monitored by ^{13}C NMR spectrometry. This revealed a new broad resonance at 44 ppm that replaced the starting material (20.1 ppm), after adding base. This new resonance was believed to correspond to the four membered-ring intermediate **3.29** based on chemical shift and line width. The ^{13}C-^{11}B-correlation spectroscopy might be another piece of strong evidence. After water was added as the electrophile, a new peak at 38.4 ppm replaced the previously broad peak at 44 ppm. The peak at 38.4 ppm was confirmed to be the cyclized product **3.30** after being isolated. An additional mechanistic experiment employed ^{13}C labeled alkene **3.31**, which showed up at 114.5 ppm due to its double bond character. After subjection of alkene **3.31** to the reaction conditions, the sharp peak at 114.5 ppm vanished immediately, and a new broad peak

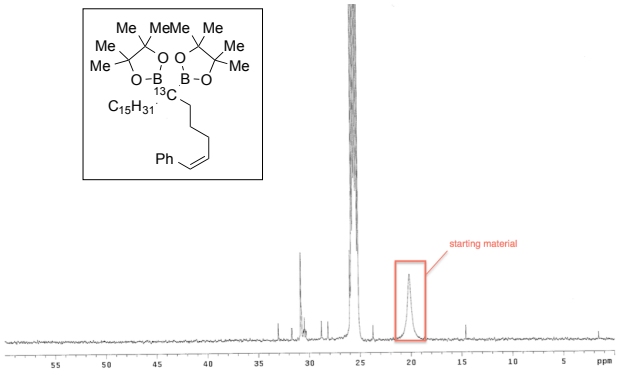
emerged at 26.9 ppm. Of note, carbon signals normally are not broad unless they are coordinated to a boron atom (quadrupole effects). The chemical shift and peak shape matched very well with a four membered-ring intermediate **3.32**, which supported our hypothesis. After the reaction was quenched with D_2O, the broad peak at 26.9 ppm disappeared immediately, and a triplet showed up at 20.6 ppm. This peak indicated the formation of the cyclized five-membered ring product **3.33**, with the splitting pattern attributed to the incorporation of deuterium.

Scheme 3.9 ^{13}C NMR Studies Supporting Four-membered Ring Intermediates

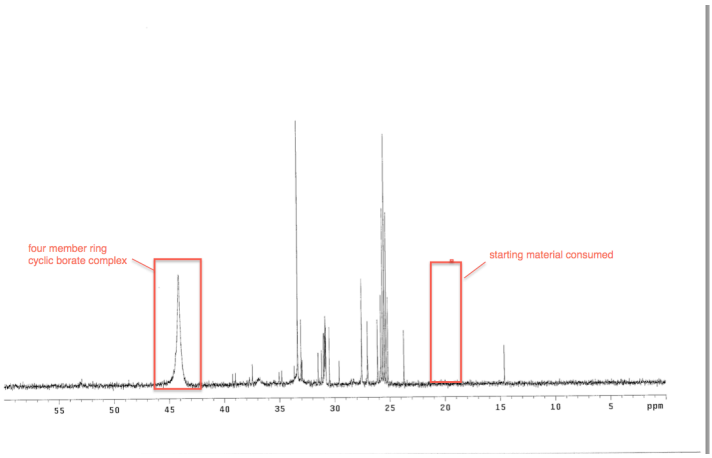


^{13}C NMR Spectra of the Reaction Mixture (125 MHz, THF-d_8, δ 10-60 ppm):

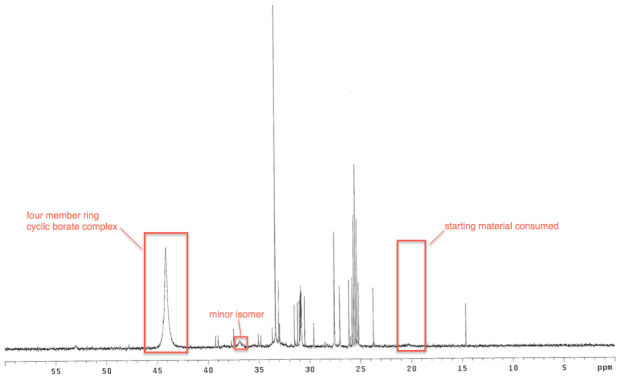
i. Diboronate ester **3.28**



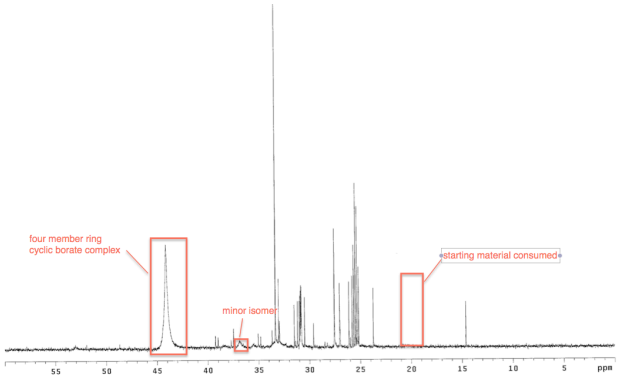
ii. **3.28** and KO^{t}Bu for 30 minutes



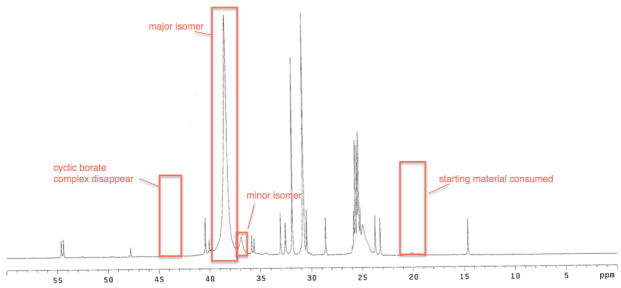
iii. **3.28** and KO^{t}Bu for 180 minutes



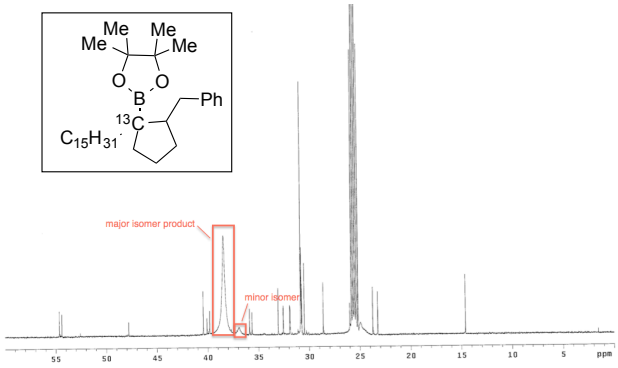
iv. **3.28** and KOtBu for 7 hours

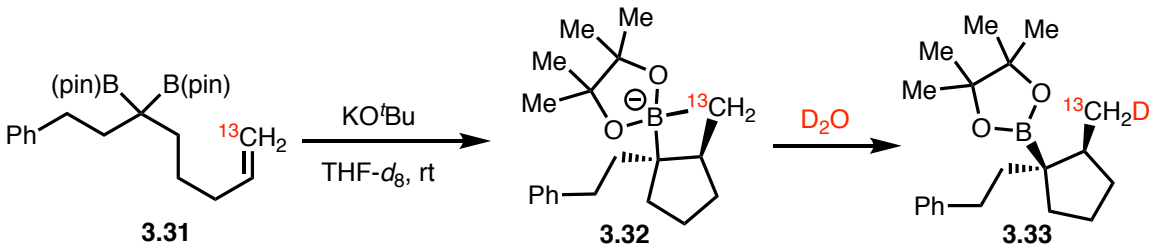


v. 1 minute after H_2O was added



vi. Isolated product, **3.30**





3.31

^{13}C δ = 114.5 ppm
(sharp)

3.32

^{13}C δ = 26.9 ppm
(broad)

3.33

^{13}C δ = 20.6 ppm
(triplet)

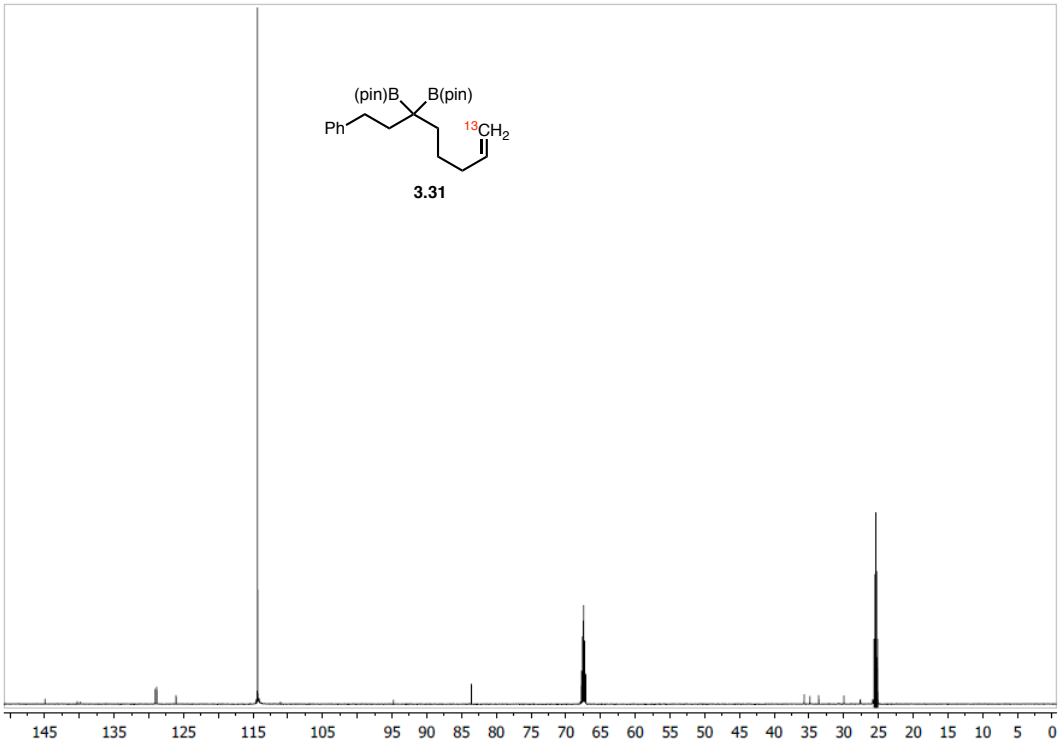


Figure 1 - ^{13}C labeled starting material (3.31) in d_8-THF

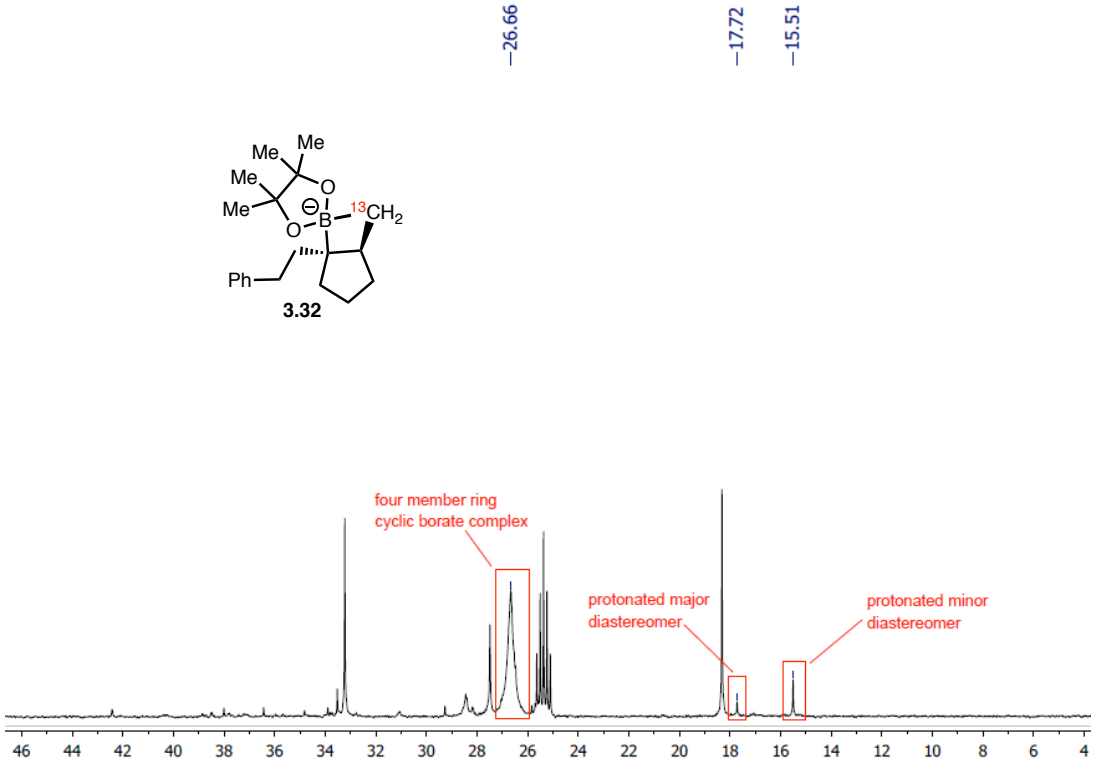


Figure 2 – 3.31 with KO*t*Bu for 20 minutes in d_8-THF (zoomed in on significant region for clarity)

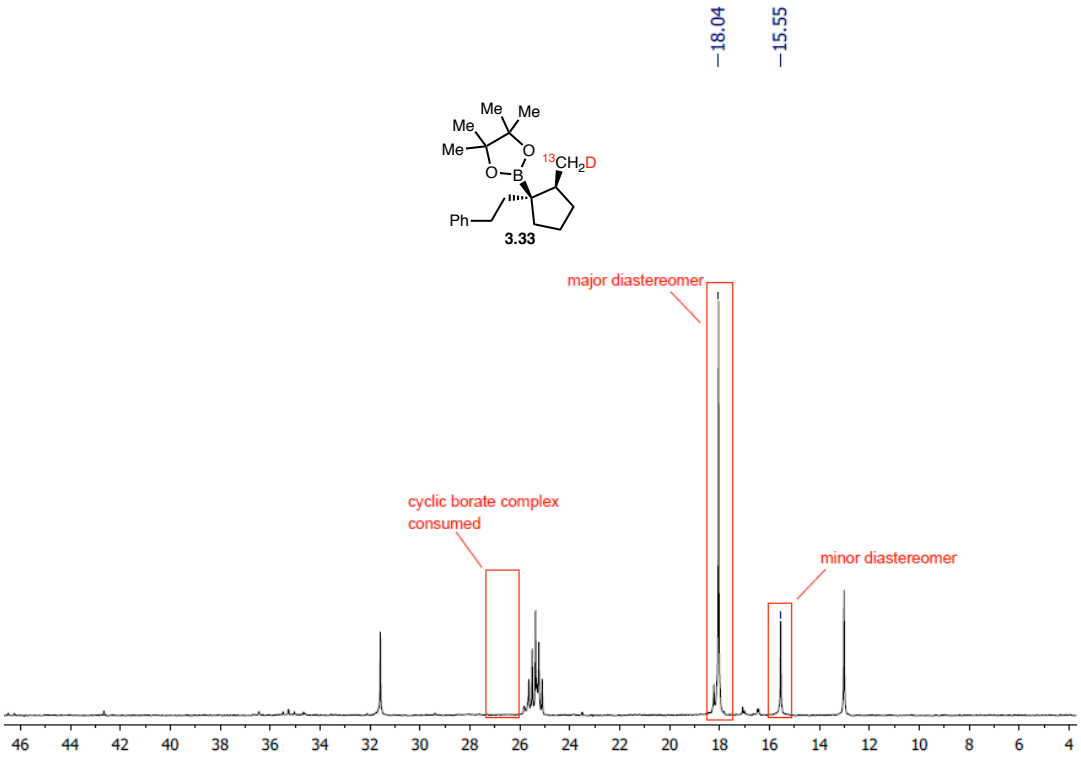


Figure 3 – 1 minute after addition of H_2O

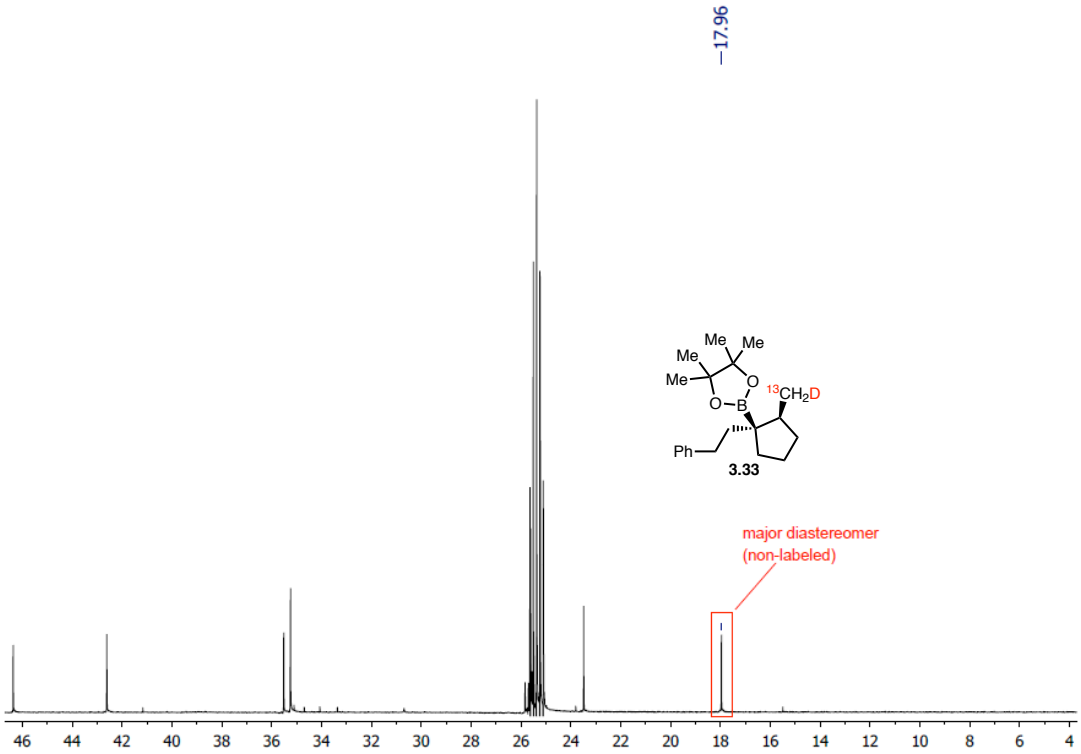


Figure 4 - Isolated major product (non-^{13}C labeled) in d_8-THF

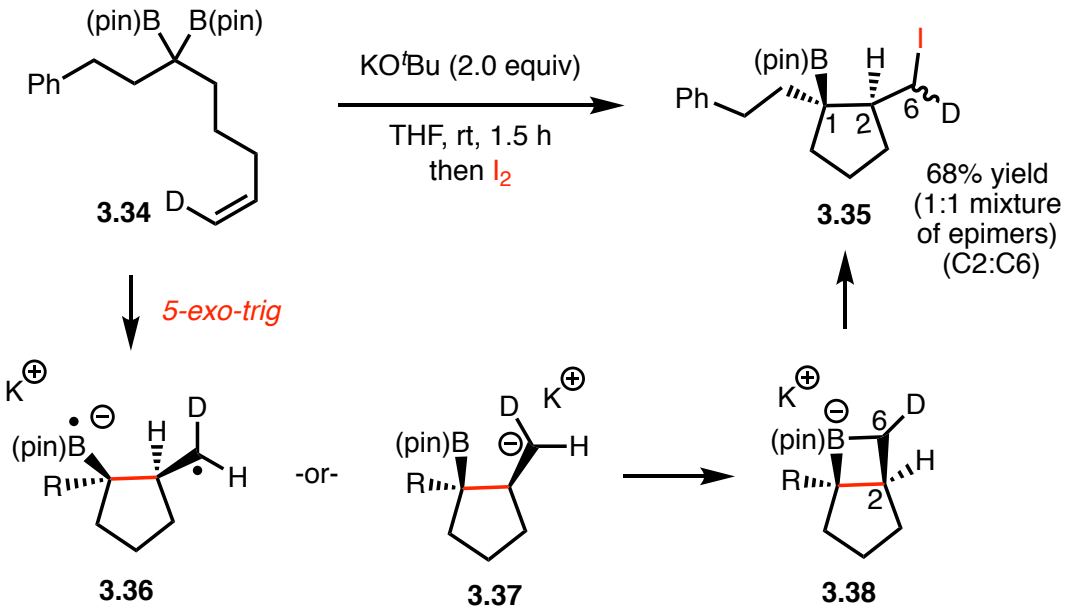
3.4.2 Distinguishing between Radical and Anionic Pathways

A very revealing experiment was performed below, starting from deuterium labeled *cis*-alkene **3.34**. This compound was treated with KO^{t}Bu and THF for 3 hours to generate four-membered ring intermediate **3.38**, followed by trapping with I_2 to afford deuterium incorporated cyclized product **3.35**. Although the diastereoselectivity is high between C1 and C2 carbons, the stereocenter at C6 was formed non-selectively, resulting in epimers in a ratio of 1:1. According to literature, the trapping of electrophiles from

boron-ate complexes usually occurs through a stereoinvertive process.[69] This indicated that the stereocenter at C6 position was not formed selectively during the formation of four-membered ring intermediate **3.38**. We proposed two possible pathways leading to this stereochemical outcome (Scheme 3.10). The first pathway is a pathway involving radical intermediates. The boron-stabilized carbanion, generated from 1,1-diborylalkane **3.34** and KO^{t}Bu**,** might undergo homolysis to form diradicals between carbon and boron atoms. The carbon radical would then react with terminal alkene to give primary radical species **3.36**, which does not have a stereogenic C6 carbon center. Alternatively, the carbanion generated from base-promoted deborylation might add to the alkene through a two-electron process, leading to primary carbanion **3.37**, which then undergoes fast racemization to deliver two epimers.

[69] Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2011,** *133*, 16794-16797.

Scheme 3.7 Two Possible Pathways for Deborylative Cyclization

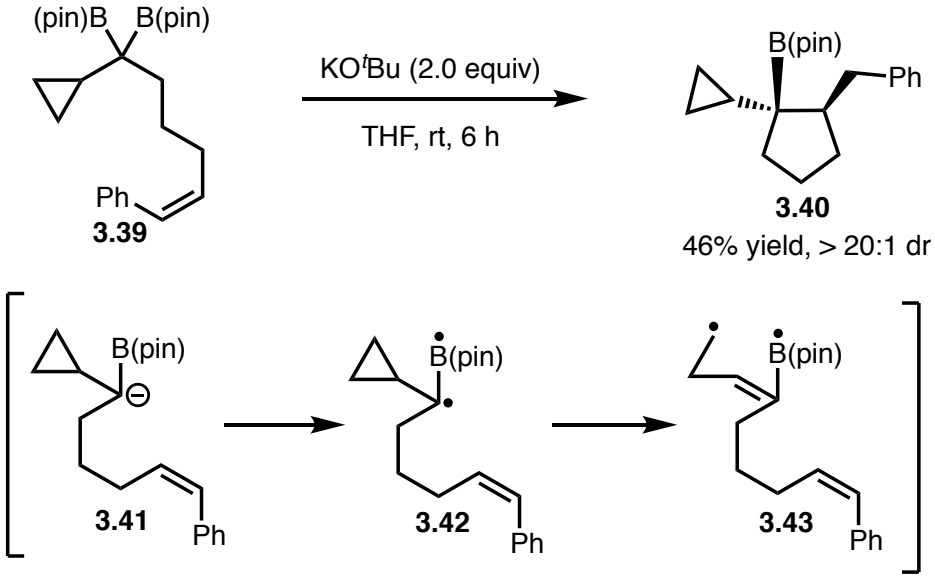


To distinguish between these two possible pathways, we designed 1,1-diboryl alkane substrate **3.39** with a tethered cyclopropyl group (Scheme 3.11). If the pathway involving radical intermediates were operative, the three-membered ring would open under standard reaction conditions; while anion pathway would provide a product with the cyclopropyl group intact. The experiment result is that the cyclized product was obtained in good yield under the standard deborylative cyclization reaction conditions with the cyclopropyl ring intact. However, this result was not sufficient to rule out the radical pathway. There is a possibility that the boron alkylidene **3.41** could react by way of a thermally accessible diradical **3.42**,[70] which could open the cyclopropyl ring to

[70] Nonhebel, D. *Chem. Soc. Rev.* **1993**, 347-359.

afford **3.43**. However, with no reaction available for **3.43**, the structure might revert back to **3.42** prior to conversion to **3.40**.

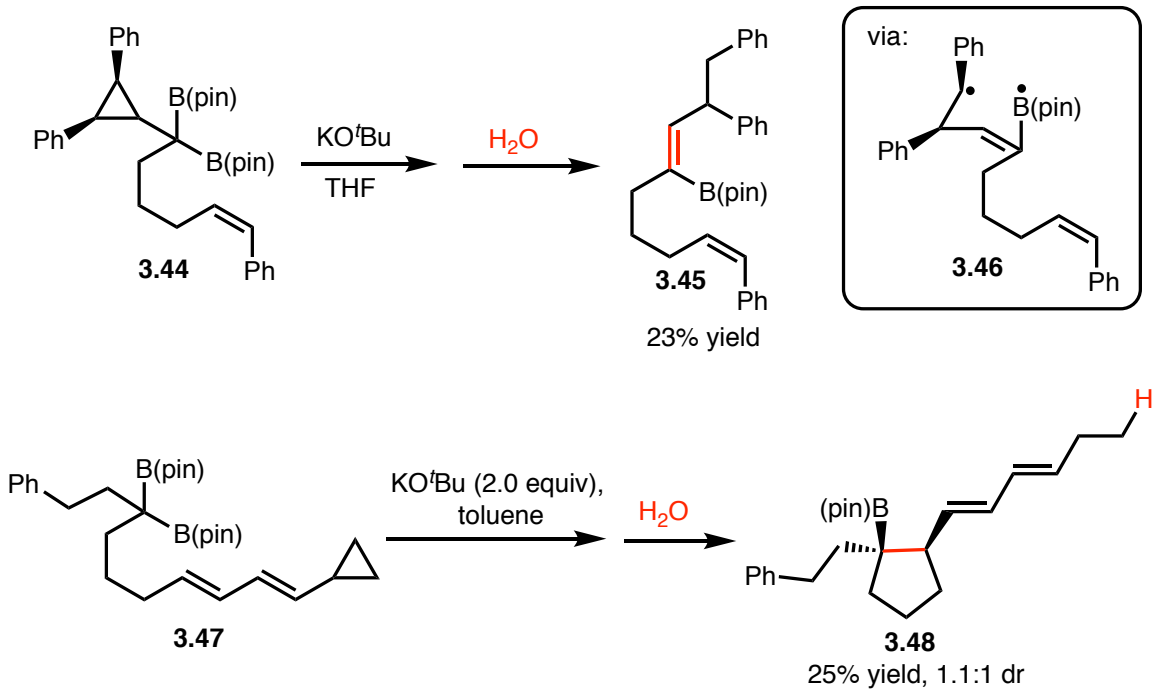
Scheme 3.11 Cyclopropyl Attached Bis(boronate) Ester as Radical Probe



To address the aforementioned concerns, we synthesized a geminal bis(boronic) ester containing a stereodefined diphenyl substituted cyclopropane ring **3.44**. If the cyclopropyl ring opened and reclosed, we might observe the epimerized product of the cyclopropyl substituent. Surprisingly, we isolated the cyclopropyl ring opened product in 23% yield. In a related fashion, a cyclopropyl group fragment included at the end of the conjugated alkene, as shown by substrate **3.47**. After subjected into the standard reaction conditions, (**3.47**) afforded the ring-opened product **3.48** in 25% yield and 1.1:1 dr.

However, since Bailey and coworkers demonstrated that lithium anions could open cyclopropane rings,[71] no definite conclusion could be drawn here.

Scheme 3.12 More Substrates as Radical Probes



To gain further information about the properties of the intermediate carbanion, we undertook additional investigations. Enantioenriched secondary alkyl halide **3.50** was treated with the deborylative alkylation conditions. The desired product was isolated in 49% yield, and it was shown that the electrophilic stereocenter in **3.50** reacted with inversion (Scheme 3.13). This S_N2 reaction pathway indicated that the boron stabilized

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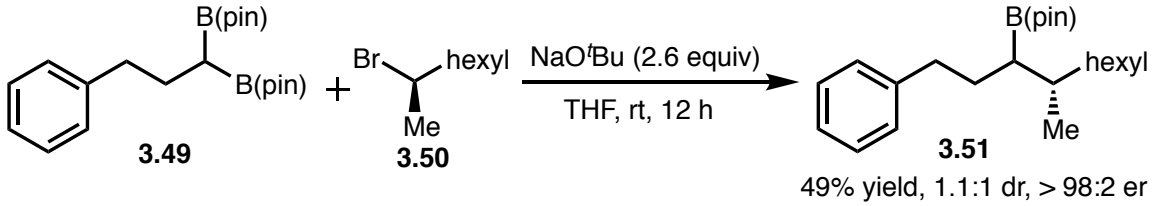
[71] Bailey, W. F.; Gavaskar, K. V. *Tetrahedron* **1994,** *50*, 5957-5970.

carbanion did not react through single electron transfer pathway, instead, a two-electron pathway was most likely operating.

Scheme 3.13 Radical Probe Experiment



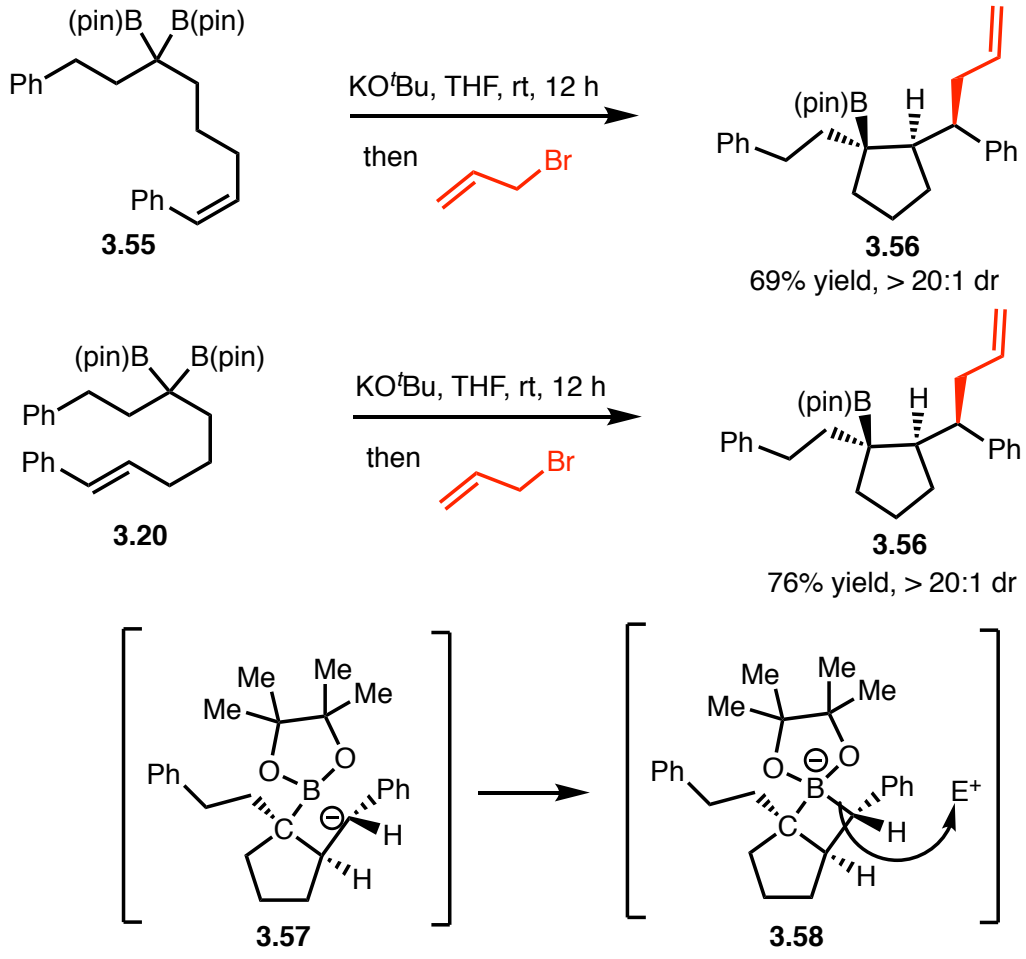
3.4.3 Concerted or Stepwise 2+2 Pathway

For the anionic pathway, two possibilities were considered. The first one is that the anion could add to the unactivated alkene through a stepwise pathway. The second is that the boron alkylidene might react with the alkene in a 2+2 concerted way. To determine which pathway is more likely the dominant one, we designed the following experiments. The *cis* and *trans*-styrene derivatives **3.55** and **3.20** were synthesized. If a 2+2 concerted pathway is the operating one, after cyclization and trapping with allyl bromide, two different stereoisomers would be anticipated, assuming that trapping with electrophiles occurs in a stereoinvertive fashion.[72] However, after subjecting these two substrates to the reaction conditions in parallel, we obtained the stereoconverged product **3.56**. This stereochemical outcome suggested that the deborylative cyclization reaction

[72] Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2011,** *133*, 16794-16797.

went through a two-electron, stepwise pathway. To explain the origin of this stereochemical outcome, we proposed that after generation of benzylic carbanion **3.57**, carbon-carbon bond rotational would occur, and the phenyl group would likely avoid eclipsing interactions with the cyclopentane ring. This effect would result in the four-membered ring intermediate configuration **3.58** as demonstrated in Scheme 3.14, which after reacting with allyl bromide would lead to the desired product **3.56**.

Scheme 3.14 Experiments to Differentiate between Concerted and Stepwise Pathway

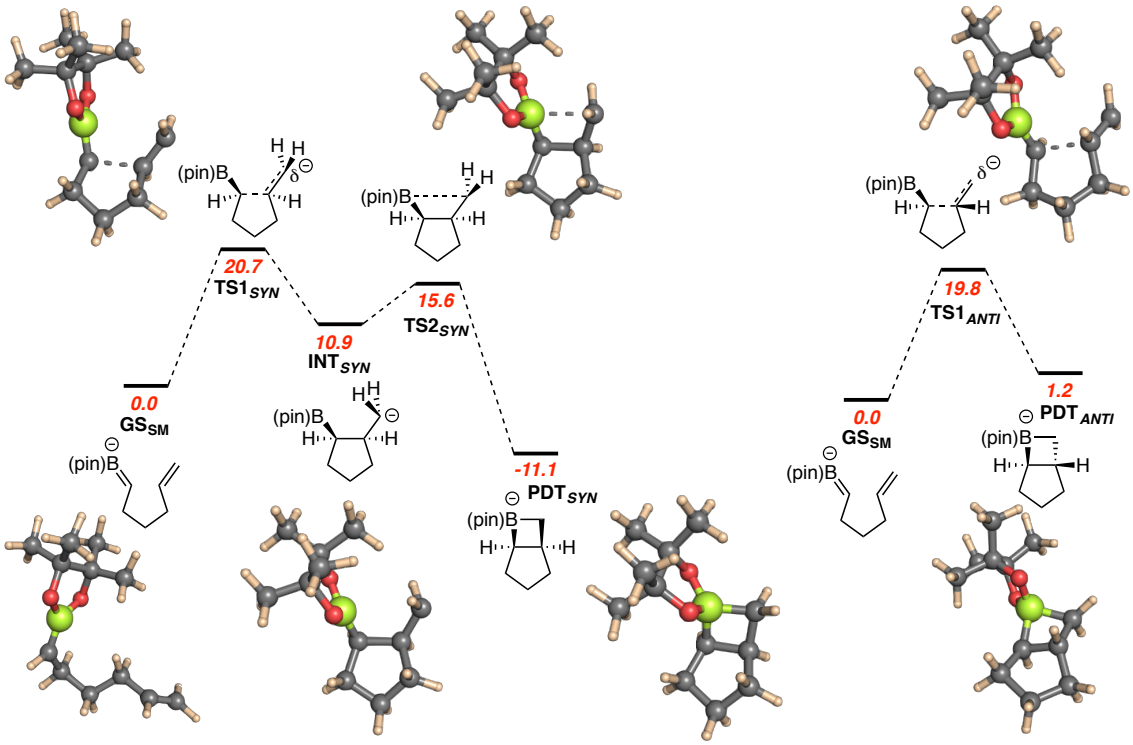


3.4.4 DFT Analysis of the Boron Alkylidene-alkene [2+2]-Cycloadddition Reaction

To gain more insight about the feasibility of the proposed stepwise reaction, collaborator Professor Fredrik Haeffner performed computational calculations for this transformation. From the same starting material boron alkylidene, the transition state energy for both the *cis* and *trans* intermediates are very similar (20.7 and 19.8 kcal/mol respectively). After cyclization, a primary carbanion INTsyn (10.9 kcal/mol) was generated, and carbon-carbon bond rotation explained the stereoconverged products **3.35** and **3.56** we observed before. The big difference between the *cis* pathway (leading to major product) and *trans* pathway (leading to minor product) is the energy of the four-membered ring intermediate PDTsyn (-11.1 kcal/mol) and PDTanti (1.2 kcal/mol). This difference in energy supported our hypothesis that the *cis* four-membered ring intermediate is stable and can persist until trapped by electrophiles. The *trans* intermediate is so unstable that it is likely quenched by adventitious water during the reaction course. This theory was further supported by comparison between products **3.8** and **3.10**, where the *trans* minor intermediate was trapped with water, becoming a byproduct, and leading to a higher diastereoselectivity of **3.8** relative to product **3.10**. Another possibility worth considering is that the *trans* minor four-membered ring intermediate might never form because of high-energy barrier of the *trans* five-four fused

bicyclic ring systems. The structure of *trans* minor intermediate might be five-membered ring with its carbanion stabilized by the potassium cation. This intermediate was then quenched by water, leading to the byproduct.

Scheme 3.15 DFT Analysis of the Boron Alkylidene-alkene 2+2 Cycloadddition Reaction



3.5 Total Synthesis of Aphanamal

My coworker Max Deaton demonstrated the synthetic utility of this methodology by accomplishing the total synthesis of natural product Aphanamal.[73] Since this synthesis was already discussed in his thesis,[74] it will not be explained in detail here. Of note, three stereocenters were established in one step for product **3.60** with high diastereoselectivity (> 7:1) from readily accesible geminal bis(boronic) ester **3.59**.

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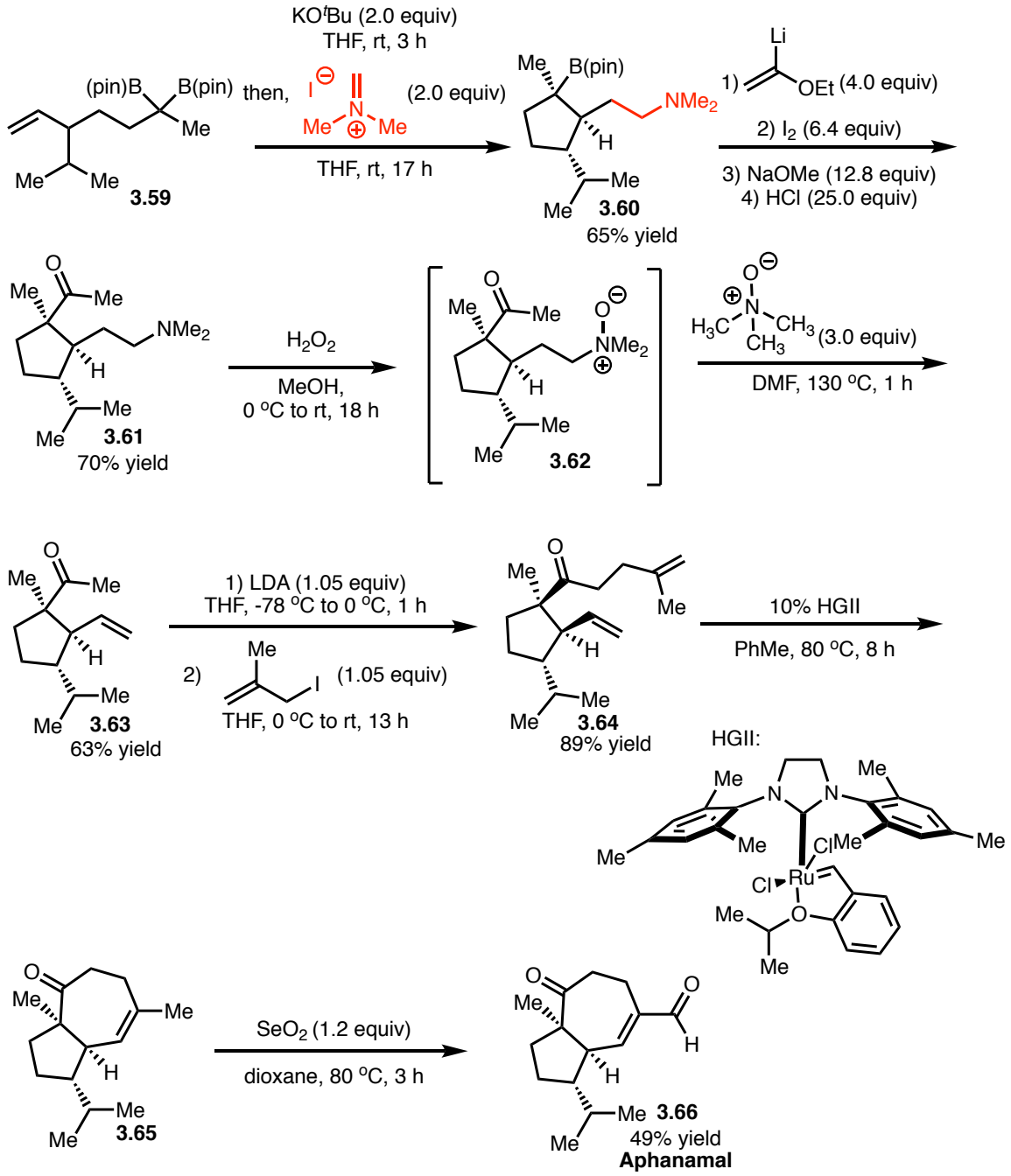
[73] (a) Mehta, G.; Krishnamurthy, N.; Karra, S. R. *J. Chem. Soc. Chem. Commun.* **1989**, 129-130. (b) Hansson, T.; Wickberg, B. *J. Org. Chem.* **1992**, *57*, 5370-5376. (c) Harmata, M.; Carter, K. W. *Tetrahedron Lett.* **1997**, *38*, 7985-8120. (d) Wender, P. A.; Zhang, L. *Org. Lett.* **2000**, *2*, 2323-2326. (e) Ferrara, S. J.; Burton, J. W. *Chem. Eur. J.* **2016**, *22*, 11597-11600.

[74] Deaton, Timothy Maxwell. "A Boron Alkylidene-Alkene Cycloaddition Reaction: Application to the Synthesis of Aphanamal", MS, Boston College, 2017. http://hdl.handle.net/2345/bc-ir:107597.

Scheme 3.16 Total Synthesis of Natural Product Aphanamal



3.6 Conclusions

We have developed a boron alkylidene-alkene cyclization reaction to construct synthetically versatile five-membered ring containing boronic esters. After mechanistic studies, we believe that this deborylative cylization reaction possibily occur by a two-electron, stepwise pathway. DFT calculations were also performed to help us gain more insight into this transformation.

3.7 Experimental Sections

3.7.1 General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), or a Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm, THF-d_8: 3.58 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qi = quintet, sx = sextet, sp = septet, m = multiplet, br = broad), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.0 ppm, THF-d_8: 67.57 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers

(cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution mass spectrometry (DART+) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA.

Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 – 400 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), phosphomolybdic acid (PMA) in ethanol and ceric ammonium molybdate (CAM) in ethanol.

Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector.

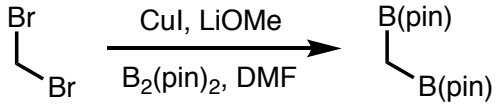
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether, dichloromethane and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon.

Bis(pinacolato)diboron was generously donated by Allychem Co., Ltd. and used without further purification. Triethylamine was purchased from Alfa Aesar and distilled over calcium hydride prior to use. The following reagents were purchased and used without purification: copper(I) iodide (CuI) (Aldrich), lithium 2,2,6,6-tetramethylpiperidide (LTMP) (Aldrich), sodium *tert*-butoxide (NaO*t*-Bu)

(Strem), palmitic acid-1-^{13}C (Cambridge Isotope Laboratories), and *N*,*N*-dimethylformamide (DMF) (Acros). All other reagents were purchased from either Aldrich, Alfa Aesar or Acros and used without further purification.

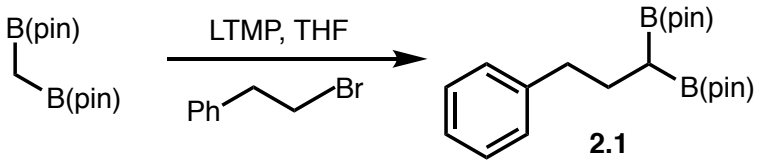
3.7.2 Representative Procedures for Preparation of *Geminal* Diboronate Esters

Method A:



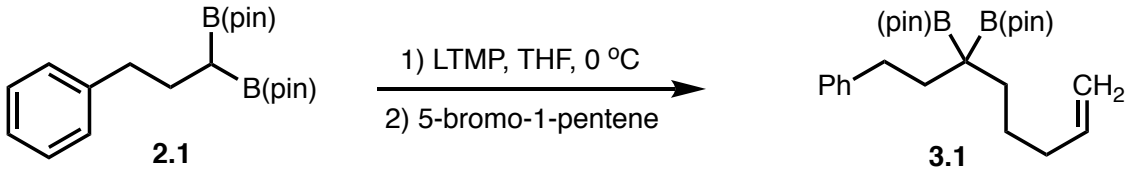
In the glove box, an oven-dried 500 mL round-bottom flask with magnetic stirring bar was charged with CuI (1.428 g, 7.500 mmol), LiOMe (8.543 g, 225 mmol) and $B_2(pin)_2$ (38.09 g, 150.0 mmol). The flask was sealed with a rubber septum, removed from the glove box, followed by the addition of DMF (150 mL) under N_2. After stirring at room temperature for 10 min, dibromomethane (10.53 mL, 150.0 mmol) was added *via* syringe at room temperature. The reaction mixture was allowed to stir at room temperature for 12 hours. Upon completion, 200 mL diethyl ether was added. The slurry was filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture in DMF was diluted with hexanes (300 mL), washed with H_2O (75 mL × 4), dried over Na_2SO_4, and then concentrated *in vacuo*. The desired product bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane was obtained as a white solid (15.72 g, 78%) and used without further purification.

Method B:



In the glove box, an oven-dried 25 mL round-bottom flask with magnetic stir bar was charged with LTMP (773 mg, 5.25 mmol). The flask was sealed with a rubber septum, removed from the glove box, followed by the addition of THF (20 mL) under N_2. The reaction mixture was cooled to 0 ^oC, and a solution of 1,1-diborylmethane (1.34 g, 5.00 mmol) in THF (5 mL) was added *via* syringe and the mixture was allowed to stir at 0 °C for 10 minutes. (2-Bromoethyl)benzene (751 μL, 5.50 mmol) was added dropwise and the reaction was allowed to stir at 0 ^oC for 15 min. Upon completion, the reaction mixture was warmed to room temperature, filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 9:1) to afford the desired product **2.1** as a colorless oil (1.54 g, 83%)

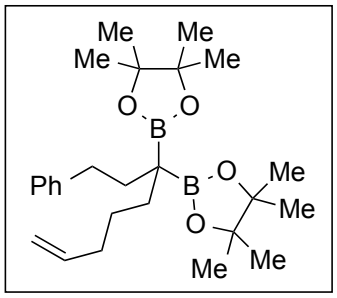
Method C:



In the glove box, an oven-dried 2-dram vial with magnetic stir bar was charged with LTMP (147 mg, 1.0 mmol). The flask was sealed with a rubber septum, removed

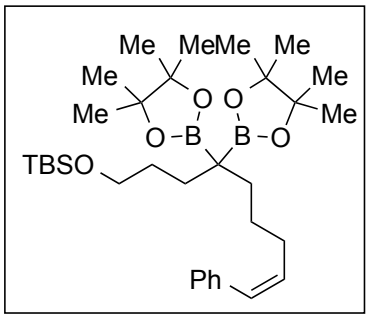
from the glove box, followed by the addition of THF (2 mL) under N_2. The reaction mixture was cooled to 0 ^oC, and was transferred into a solution of 1,1-diboronate ester (372 mg, 1.00 mmol) in THF (2 mL) *via* syringe at 0 °C and the mixture was allowed to stir at 0 °C for 10 minutes. Then, 5-bromopent-1-ene (120 mL, 1.0 mmol) was added into the above mixture *via* syringe at 0 °C. The reaction mixture was allowed to stir at 0 ^oC for 15 min, then warmed to room temperature, filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: diethyl ether = 20:1) to afford **3.1** as a white solid (360 mg, 84%).

3.7.3 Full Characterization of geminal-Diboronate Esters



2,2'-(1-phenyloct-7-ene-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.1). The reaction was performed according to *Representative Procedure (Method C)* with diboronate ester **2.1** (372 mg, 1.0 mmol), LTMP (147 mg, 1.0 mmol), 5-bromo-1-pentene (120 mL, 1.0 mmol) and THF (4 mL). The crude reaction mixture was purified by column chromatography on silica gel (20:1 hexanes/diethyl ether, stain in CAM) to afford a white solid (360 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.23 (m, 2H), 7.20-7.19 (m, 2H), 7.15-7.12 (m, 1H), 5.86 (ddt, *J* = 17.1, 10.3, 6.9 Hz, 1H), 5.01 (ddt, *J* = 17.1, 2.0, 1.5 Hz, 1H), 4.93 (ddt, *J* = 10.3, 2.4, 1.0 Hz , 1H), 2.52-2.49 (m, 2H), 2.10-2.06 (m, 2H), 1.91-1.88 (m, 2H), 1.74-1.71 (m, 2H), 1.41-1.35

(m, 2H), 1.23 (s, 24H); ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.69; The ^{1}H NMR spectrum was in accord with previously reported data.[75]



(*Z*)-*tert*-butyldimethyl((9-phenyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)non-8-en-1-yl)oxy)silane) (S3.1). Prepared according to *Representative Procedure (Method C)* with LTMP (177 mg, 1.0 mmol), diboronate ester **S3.4** (412 mg, 1.0 mmol), (3-bromopropoxy)-*tert*-butyldimethylsilane (253 mg, 1.0 mmol), and THF (5 mL). The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 50:1) to afford the desired product as a white solid (455 mg, 77%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33 – 7.22 (m, 4H), 7.21 – 7.16 (m,1H), δ 6.36 (d, *J* = 11.7 Hz, 1H), 5.68 (dt, *J* = 11.6, 7.3 Hz, 1H), 3.58 (t, *J* = 7.2 Hz, 2H), 2.31 (dt, *J* = 8.4, 6.5 Hz, 2H), 1.70 – 1.62 (m, 2H), 1.60 – 1.55 (m, 2H), 1.51 – 1.44 (m, 2H), 1.39 – 1.34 (m, 2H), 1.21 (s, 24H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.84, 133.44, 128.73, 128.38, 128.02, 126.27, 82.92, 64.32, 30.63, 29.56, 28.95, 27.60, 26.01, 24.74, 24.70, 18.40, -5.18; ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.17; IR (neat): 2977.1 (m), 2929.4 (m), 2857.6 (w), 1461.6 (w), 1378.1.5 (m), 1371.8 (m), 1355.5 (m), 1307.2 (m), 1139.6 (s), 973.4 (w), 853.3 (m), 853.8 (m), 774.4 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{33}{}^{1}H_{59}{}^{11}B_2{}^{16}O_5{}^{28}Si_1$ $[M+H]^+$: calculated: 585.4318, found: 585.4309.

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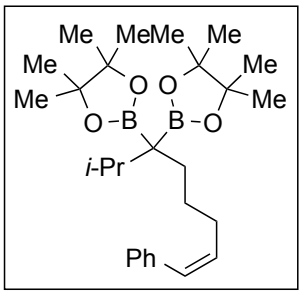
[75] K. Hong, X. Liu, and J. P. Morken *J. Am. Chem. Soc.* **2014**, *136,* 10581-10584.



(*Z*)-2,2'-(2-methyl-8-phenyloct-7-ene-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S3.2). The reaction was performed according to *Representative Procedure (Method C)* with 2,2'-(2-methylpropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (509 mg, 1.6 mmol, made according to previous procedure[76]), LTMP (236 mg, 1.60 mmol), (*Z*)-(5-bromopent-1-en-1-yl)benzene (361 mg, 1.60 mmol) and THF (8 mL). The crude reaction mixture was purified by column chromatography on silica gel (100:1 – 50:1 hexanes/ethyl acetate, stain in CAM) to afford a white solid (530 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.25 (m, 4H), 7.19 (m, 1H), 6.36 (d, J = 11.7, 1H), 5.71 (dt, J = 11.6, 7.2 Hz, 1H), 2.31 (qd, J = 7.4, 1.8 Hz, 2H), 2.04 (p, J = 6.8 Hz, 1H), 1.68 – 1.59 (m, 2H), 1.59 – 1.45 (m, 2H), 1.21 (s, 24H), 0.98 (d, J = 6.8 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.94, 133.70, 128.76, 128.24, 128.01, 126.24, 82.56, 30.04, 29.75, 29.21, 28.42, 24.81, 24.77, 21.29; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.881; IR (neat): 2976.8 (m), 2929.6 (m), 1728.5 (w), 1459.8 (w), 1378.0 (m), 1370.6 (m), 1296.1 (s), 1264.8 (m), 1215.1 (w), 1140.7 (s), 972.8 (w), 854.0 (w), 757.8 (s), 699.5 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{27}{}^{1}H_{45}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 455.3504, found: 455.3504.

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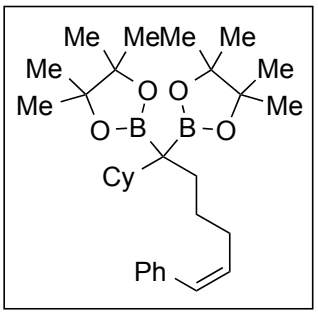
[76] Li, H.; Shangguan, X.; Zhang, Z.; Huang, S.; Zhang, Y.; Wang, J. *Org. Lett.* **2014**, *16*, 448-451.



(*Z*)-2,2'-(1-cyclohexyl-6-phenylhex-5-ene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**S3.3**). The reaction was performed according to *Representative Procedure (Method C)* with 2,2'-(cyclohexylmethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (350 mg, 1.0 mmol; made according to previously reported procedure[77]), LTMP (147 mg, 1.0 mmol), (*Z*)-(5-bromopent-1-en-1-yl)benzene (225 mg, 1.60 mmol) and THF (5 mL). The crude reaction mixture was purified by column chromatography on silica gel (100:1 – 50:1 hexanes/ethyl acetate, stain in CAM) to afford a colorless oil (378 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.28 (m, 4H), 7.31 – 7.15 (m, 1H), 6.37 (d, *J* = 11.6, 1H), 5.72 (dt, *J* = 11.6, 7.2 Hz, 1H), 2.30 (qd, *J* = 7.4, 1.8 Hz, 2H), 1.80 – 1.73 (m, 2H), 1.73 – 1.58 (m, 6H), 1.57 – 1.46 (m, 2H), 1.21 (s, 24H), 1.31 – 1.02 (m, 4H), 0.91 – 0.82 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.97, 133.80, 128.77, 128.20, 128.02, 126.24, 82.57, 40.24, 31.53, 30.13, 29.41, 28.66, 27.42, 26.96, 24.82, 24.80; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.59; IR (neat): 2977.4 (m), 2925.9 (m), 2851.9 (w), 1447.1 (w), 1377.5 (m), 1370.6 (m), 1344.1 (m), 1293.8 (m), 1137.7 (s), 974.0 (w), 850.9 (w), 699.5 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{30}{}^{1}H_{49}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 495.3817, found: 495.3819.

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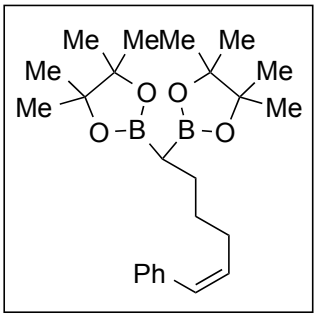
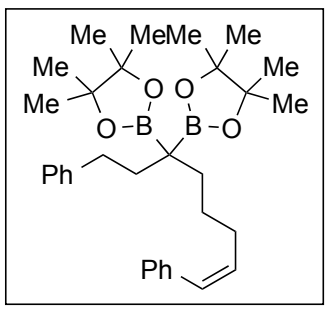
[77] K. Hong, X. Liu, and J. P. Morken *J. Am. Chem. Soc.* **2014**, *136,* 10581-10584.

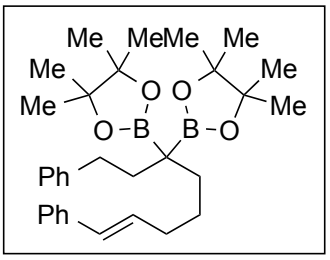


(*Z*)-2,2'-(6-phenylhex-5-ene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)) (S3.4). The reaction was performed according to *Representative Procedure (Method C)* with methyl diboronate ester (429 mg, 1.60 mmol), LTMP (236 mg, 1.60 mmol), (*Z*)-(5-bromopent-1-en-1-yl)benzene (361 mg, 1.60 mmol) and THF (8 mL). The crude reaction mixture was purified by column chromatography on silica gel (50:1 – 20:1 hexanes/ethyl acetate, stain in CAM) to afford a white solid (500 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 – 7.22 (m, 4H), 7.22 – 7.17 (m, 1H), 6.37 (d, J = 11.7 Hz, 1H), 5.67 (dt, J = 11.6, 7.3 Hz, 1H), 2.31 (qd, J = 7.5, 1.9 Hz, 2H), 1.60 (q, J = 7.8 Hz, 2H), 1.50 – 1.40 (m, 2H), 1.22 (s, 12H), 1.21 (s, 12H), 0.74 (t, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.80, 133.28, 128.70, 128.43, 128.02, 126.27, 82.90, 32.88, 28.86, 25.57, 24.83, 24.48; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.59; IR (neat): 2976.8 (m), 2927.3 (w), 1368.7 (m), 1311.6 (s), 1267.5 (m), 1214.5 (w), 1139.3 (s), 969.4 (m), 849.7 (m), 699.8 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{24}{}^{1}H_{39}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 413.3034, found: 413.3052.



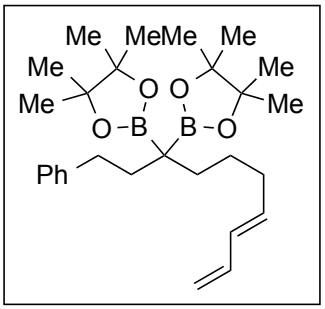
(*Z*)-2,2'-(1,8-diphenyloct-7-ene-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)) (3.55). The reaction was performed according to *Representative Procedure (Method*

C) with diboronate ester **2.1** (441 mg, 1.18 mmol), LTMP (174.5 mg, 1.18 mmol), (*Z*)-(5-bromopent-1-en-1-yl)benzene (267 mg, 1.186 mmol) and THF (6 mL). The crude reaction mixture was purified by column chromatography on silica gel (20:1 hexanes/ethyl acetate, stain in CAM) to afford a white solid (543 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.10 (m, 10H), 6.40 (d, *J* = 11.7 Hz, 1H), 5.73 (dt, *J* = 11.6, 7.3 Hz, 1H), 2.56 – 2.48 (m, 2H), 2.37 (qd, *J* = 7.4, 1.8 Hz, 2H), 1.96 – 1.88 (m, 2H), 1.82 – 1.73 (m, 2H), 1.52 – 1.41 (m, 2H), 1.24 (two sets of singlet, 24H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.72, 137.83, 133.38, 128.73, 128.53, 128.46, 128.08, 128.04, 126.32, 125.34, 82.98, 33.83, 31.92, 29.56, 28.95, 27.68, 24.78, 24.71; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.98; IR (neat): 2977.2 (m), 2928.4 (w), 1454.5 (w), 1370.5 (m), 1352.4 (m), 1308.8 (s), 1254.6 (m), 1214.1 (w), 1138.1 (s), 968.9 (w), 854.6 (w), 699.2 (m) cm^{-1}. HRMS-(DART+) for $^{12}C_{32}{}^{1}H_{47}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 517.3660, found: 517.3639.



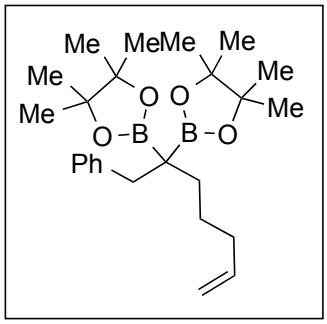
(*E*)-2,2'-(1,8-diphenyloct-7-ene-3,3-diyl)bis(4,4,5,5-tetra methyl-1,3,2-dioxaborolane) (3.20). The reaction was performed according to *Representative Procedure (Method C)* with diboronate ester **2.1** (1.0 g, 2.69 mmol), LTMP (417 mg, 2.83 mmol), (*E*)-(5-bromopent-1-en-1-yl)benzene (636 mg, 2.83 mmol) and THF (10.8 mL). The crude reaction mixture was purified by column chromatography on silica gel (20:1 hexanes/ethyl acetate, stain in CAM) to afford a white solid (543 mg, 39%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.32 – 7.22 (m, 4H),

7.23 – 7.17 (m, 3H), 7.20 – 7.11 (m, 1H), 6.40 (d, *J* = 15.7 Hz, 1H), 6.28 (dt, *J* = 15.9, 6.7 Hz, 1H), 2.56 – 2.49 (m, 2H), 2.25 (q, *J* = 6.9 Hz, 2H), 1.95 – 1.89 (m, 2H), 1.81 – 1.75 (m, 2H), 1.52 – 1.43 (m, 2H), 1.24 (s, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 143.73, 138.07, 131.42, 129.48, 128.48, 128.40, 128.09, 126.62, 125.91, 125.35, 83.00, 33.86, 33.83, 31.91, 28.77, 27.10, 24.81, 24.71; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.69; IR (neat): 2977.5 (w), 2929.4 (w), 1453.7 (w), 1378.5 (m), 1307.6 (m), 1253.4 (m), 1138.4 (s), 967.5 (w), 851.2 (w), 751.4 (m), 698.1 (w) cm^{-1}HRMS-(DART+) for $^{12}C_{32}{}^{1}H_{47}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 517.3660, found: 517.3664.



(*E*)-2,2'-(1-phenyldeca-7,9-diene-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.22). The reaction was performed according to *Representative Procedure (Method C)* with diboronate ester **2.1** (633 mg, 1.7 mmol), LTMP (250 mg, 1.7 mmol), (*E*)-7-bromohepta-1,3-diene (296 mg, 1.7 mmol) and THF (7 mL). The crude reaction mixture was purified by column chromatography on silica gel (50:1 hexanes/ethyl acetate, stain in CAM) to afford a white solid (713 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28 – 7.10 (m, 5H), 6.32 (dt, *J* = 17.0, 10.3 Hz, 1H), 6.06 (dd, *J* = 15.3, 10.3 Hz, 1H), 5.75 (dt, *J* = 14.5, 6.8 Hz, 1H), 5.08 (dd, *J* = 17.0, 1.7 Hz, 1H), 4.94 (dd, *J* = 10.1, 1.7 Hz, 1H), 2.53 – 2.47 (m, 2H), 2.11 (q, *J* = 7.2 Hz, 2H), 1.92 – 1.86 (m, 2H), 1.75 – 1.69 (m, 2H), 1.42 – 1.34 (m, 2H), 1.23 (s, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 143.74, 137.52, 135.85, 130.64, 128.48, 128.09,

125.35, 114.37, 82.99, 33.84, 33.34, 31.87, 28.76, 26.89, 24.80, 24.71; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.88; IR (neat): 2976.8 (w), 2929.1 (w), 1455.0 (w), 1378.0 (m), 1305.6 (m), 1252.2 (m), 1137.0 (s), 1003.9 (m), 852.2 (m), 699.2 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{28}{}^{1}H_{45}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 467.3504, found: 467.3519.



2,2'-(1-phenylhept-6-ene-2,2-diyl)bis(4,4,5,5-tetramethyl -1,3,2-dioxaborolane)) (S3.5). The reaction was performed according to *Representative Procedure (Method C)* with 2,2'-(2-phenylethane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (429.7mg, 1.2 mmol, made according to previous procedure[78]), LTMP (194.3 mg, 1.32 mmol), 5-bromo-1-pentene (197 mg, 1.32 mmol) and THF (6 mL). The crude reaction mixture was purified by column chromatography on silica gel (50:1 hexanes/ethyl acetate, stain in CAM) to afford a colorless oil (450 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 – 7.17 (m, 4H), 7.15 – 7.07 (m, 1H), 5.82 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 4.97 (dq, J = 17.2, 1.8 Hz, 1H), 4.90 (ddt, J = 10.2, 2.4, 1.3 Hz, 1H), 2.97 (s, 2H), 2.00 (q, J = 7.1 Hz, 2H), 1.56 – 1.51 (m, 2H), 1.49 – 1.41 (m, 2H), 1.24 (s, 12H), 1.20 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.82, 139.32, 129.70, 127.65, 125.41, 113.82, 83.16, 34.58, 34.44, 28.45, 26.77, 25.00, 24.69; IR (neat): 2978.4 (m), 2931.7 (w),

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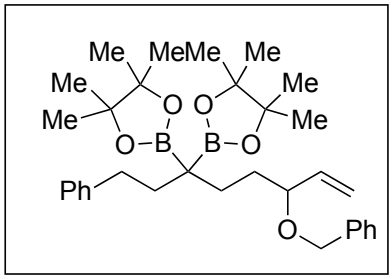
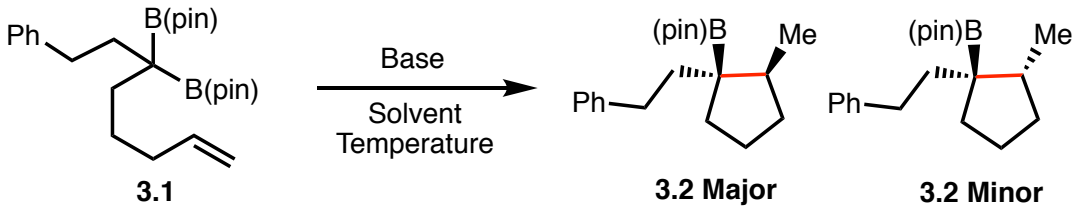
2862.9 (m), 1378.4 (m), 1353.4 (m), 1261.8 (m), 1138.8 (s), 854.3 (w), 699.9 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{25}{}^{1}H_{41}{}^{11}B_{2}{}^{16}O_{4}$ $[M+H]^{+}$: calculated: 427.3191, found: 427.3189.



2,2'-(6-(benzyloxy)-1-phenyloct-7-ene-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)) (**S3.6**). The reaction was performed according to *Representative Procedure (Method C)* with diboronate ester **2.1** (186 mg, 0.5 mmol), LTMP (73.6 mg, 0.5 mmol), 3-(benzyloxy)pent-4-en-1-yl 4-methylbenzenesulfonate (193 mg, 0.56 mmol) and THF (5 mL). The crude reaction mixture was purified by column chromatography on silica gel (100:2 – 100:4 hexanes/ethyl acetate, stain in CAM) to afford a colorless oil (220 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.30 (m, 4H), 7.26 – 7.21 (m, 3H), 7.20 – 7.16 (m, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 5.84 – 5.69 (m, 1H), 5.25 – 5.22 (m, 2H), 4.60 (d, *J* = 12.1 Hz, 1H), 4.40 (d, *J* = 12.1 Hz, 1H), 3.73 (q, *J* = 6.8 Hz, 1H), 2.50 (td, *J* = 7.3, 3.7 Hz, 2H), 1.88 (dd, *J* = 10.7, 6.9 Hz, 2H), 1.80 – 1.63 (m, 3H), 1.59 – 1.50 (m, 1H), 1.22 (s, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 143.76, 139.03, 128.51, 128.21, 128.07, 127.58, 127.20, 125.32, 117.22, 82.99, 81.33, 69.77, 33.79, 32.81, 31.96, 24.91, 24.78, 24.65; IR (neat): 2977.4 (m), 2932.1 (w), 1378.5 (w), 1370.5 (w), 1309.9 (s), 1138.56 (s), 851.8 (w), 698.5 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{33}{}^{1}H_{52}{}^{11}B_{2}{}^{16}O_{5}{}^{14}N_{1}$ $[M+NH_4]^{+}$: calculated: 564.4032, found: 564.4058.

3.7.4 Representative Procedure for Deborylative Cyclization

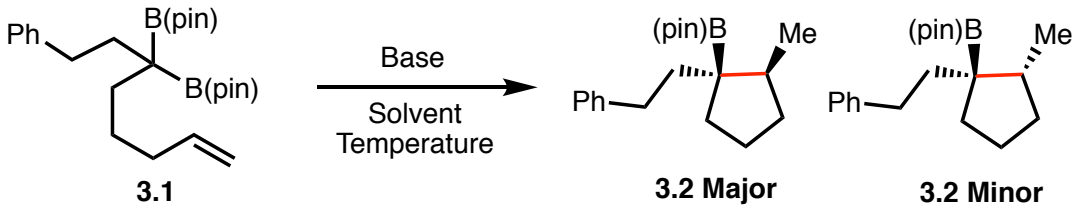


3.1 **3.2 Major** **3.2 Minor**

In the glove box, an oven-dried 2-dram vial equipped with magnetic stir bar is charged with 1,1-diboronate ester **3.1** (48.4 mg, 0.10 mmol), base (0.20 mmol) and THF (0.50 mL). The vial is sealed with a polypropylene cap, removed from the glove box, and allowed to stir at room temperature for overnight. Upon completion, the reaction mixture is diluted with wet diethyl ether (2 mL), filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture is then purified on silica gel (hexanes: ethyl acetate = 100 : 0.8) to afford the desired product **3.2** ***major*** and **3.2** ***minor***.

3.7.5 Full Optimization[a]

Table S3.1.

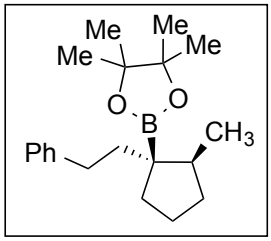


3.1 **3.2 Major** **3.2 Minor**

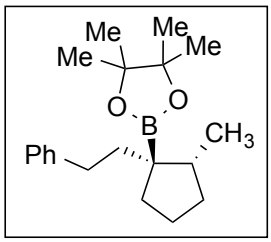
entry	base	solvent	yield (%)	d.r. (3.2 major : 3.2 minor)
1	NaO*t*-Bu	THF	12	13 : 1
2	NaO*t*-Bu	toluene	<5	N/A
3	KOMe	toluene	<5	N/A
4	KO*t*-Bu	DCE	<5	N/A
5	KO*t*-Bu	hexanes	39	2.2 : 1
6	KO*t*-Bu	THF	51	5 : 1 [b]
7	KO*t*-Bu	THF	52	4 : 1
8	KO*t*-Bu	toluene	52	2 : 1 [b]
9	KO*t*-Bu	toluene	61	1.2 : 1

[a] Reaction conditions: 1,1-diboronate ester (0.10 mmol, 0.2 M), and base (0.20 mmol). Yield refers to the isolated yield of purified material. Diastereoselectivity was determined based on NMR integration. [b] Reaction conducted at 50 °C.

3.7.6 Full Characterization of Reaction Products and Proof of Stereochemistry



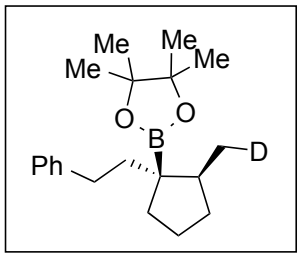
4,4,5,5-tetramethyl-2-(2-methyl-1-phenethylcyclopentyl)-1,3,2-dioxaborolane (3.2, *major diastereomer*). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **3.1** (88 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100 : 0.8) to afford the desired product as a colorless oil (32.7 mg, 52%, 4:1 dr). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28-7.25(m, 2H), 7.20 (d, J = 7.3 Hz, 2H), 7.16 (t, J = 7.3 Hz, 1H), 2.59-2.53 (m, 2H), 2.05-1.95 (m, 2H), 1.84-1.78 (m, 1H), 1.77-1.70 (m, 1H), 1.64-1.56 (m, 2H), 1.40-1.22 (m, 3H), 1.27 (12H, s, overlap), 1.00 (d, J = 6.9 Hz, 3H) ; ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.57; The ^{1}H NMR spectrum was in accord with previously reported data.[79]



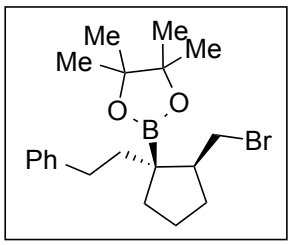
4,4,5,5-tetramethyl-2-(1-phenyltetradecan-2-yl)-1,3,2-dioxaborolane (3.2, *minor diastereomer*). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (t, J = 7.3 Hz, 2H), 7.21 (d, J = 7.3 Hz, 2H), 7.18-7.15 (m,

[79] K. Hong, X. Liu, and J. P. Morken *J. Am. Chem. Soc.* **2014**, *136,* 10581-10584.

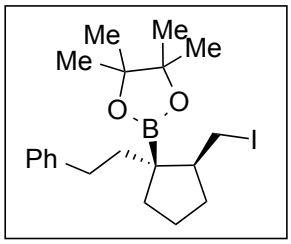
1H), 2.58-2.49 (m, 2H), 2.04 (sx, J = 7.3 Hz, 1H), 1.89-1.83 (m, 1H), 1.79-1.54 (m, 5H), 1.44-1.36 (m, 1H), 1.31-1.24 (m, 1H), 1.27 (s, overlap, 12H), 0.91 (dd, J = 7.3, 1.4 Hz, 3H); The ^{1}H NMR spectrum was in accord with previously reported data.[8]



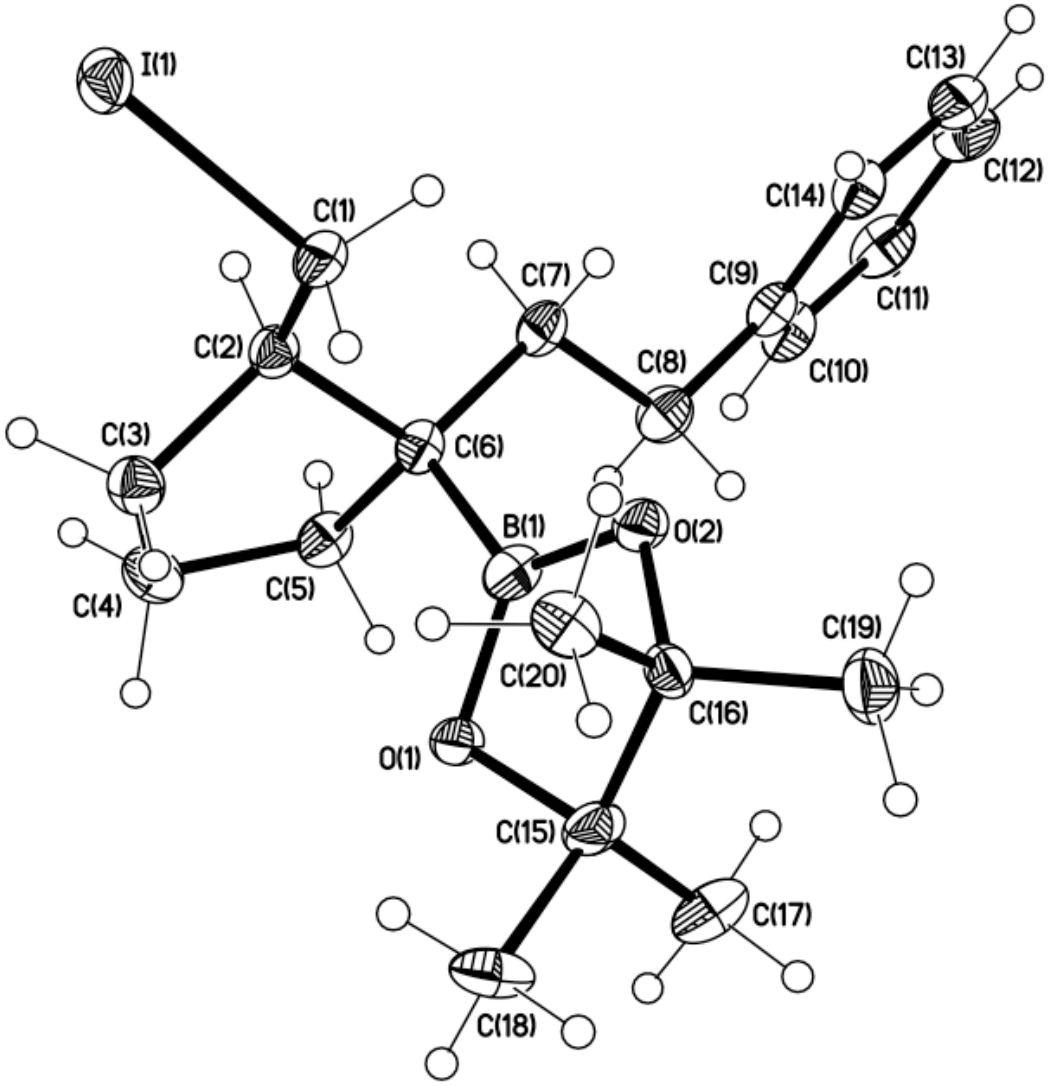
4,4,5,5-tetramethyl-2-((1*R*,2*S*)-2-(methyl-*d*)-1-phenethylcyclopentyl)-1,3,2-dioxaborolane (3.7). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **3.1** (88 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). Upon completion, the reaction mixture was quenched with D_2O (100 mL, 5.0 mmol), then diluted with diethyl ether (2 mL) and filtered through a silica gel plug, rinsing with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a colorless oil (28.1 mg, 45%, > 20:1 dr). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (t, J = 7.6 Hz, 2H), 7.23 – 7.14 (m, 3H), 2.63 – 2.50 (m, 2H), 2.07 – 1.92 (m, 2H), 1.86 – 1.68 (m, 2H), 1.63 – 1.55 (m, 2H), 1.39 – 1.20 (m, 3H), 1.27 (s, 12H), 0.99 (d, J = 7.0, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.88, 128.30, 128.19, 125.40, 125.40, 82.89, 44.93, 41.24, 34.26, 34.19, 34.14, 25.28, 24.82, 22.70, 17.63, 17.50, 17.37; IR (neat): 2977.4 (m), 2931.9 (m), 2857.6 (w), 1730.2 (w), 1454.4 (w), 1387.8 (m), 1301.7 (m), 1195.1 (w), 1143.6 (s), 966.8 (w), 855.5 (w), 748.8 (w), 698.9 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{20}{}^{1}H_{31}{}^{2}D_{1}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 316.2558, found: 316.2560.

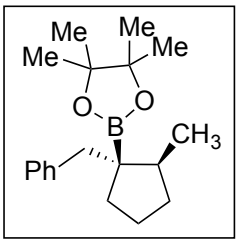


2-((1*R*,2*S*)-2-(bromomethyl)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.8). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **3.1** (88 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). Upon completion, the reaction mixture was quenched with NBS (71.2 mg, 0.4 mmol) in anhydrous THF (1 mL), then diluted with diethyl ether (2 mL) and filtered through a silica gel plug, rinsing with diethyl ether. Filtrate was then concentrated *in vacuo* and crude purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a white solid (40.3 mg, 51.2%, >20:1 dr). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.23 (m, 3H), 7.18 (dd, *J* = 7.7, 1.1 Hz, 2H), 3.72 (dd, *J* = 9.6, 3.7 Hz, 1H), 3.37 (dd, *J* = 11.4, 9.6 Hz, 1H), 2.62 – 2.50 (m, 2H), 2.18 – 2.04 (m, 2H), 2.06 – 1.91 (m, 2H), 1.79 – 1.56 (m, 2H), 1.51 – 1.37 (m, 3H), 1.26 (d, *J* = 1.6 Hz, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.13, 128.30, 128.23, 125.64, 83.31, 53.24, 41.18, 37.96, 35.71, 33.87, 32.22, 25.10, 24.82, 22.35; ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.08; IR (neat): 2976.4 (m), 2956.2 (m), 2932.3 (m), 2868.7 (w), 1454.3 (w), 1381.0 (m), 1312.3 (m), 1210.3 (m), 1142.9 (s), 967.1 (w), 855.0 (w), 748.5 (w), 698.8 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{20}{}^{1}H_{31}{}^{11}B_{1}{}^{79}Br_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 393.1601, found: 393.1608.



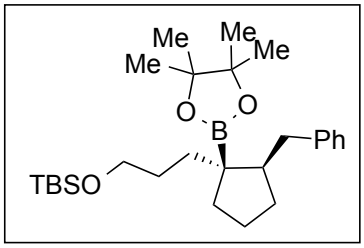
2-((1*R*,2*S*)-2-(iodomethyl)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.9). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **3.1** (88 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). Upon completion, the reaction mixture was quenched with I_2 (101.5 mg, 0.4 mmol) in anhydrous THF (1 mL), then diluted with diethyl ether (2 mL) and filtered through a silica gel plug, rinsing with diethyl ether. Filtrate was then concentrated *in vacuo* and the crude residue purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a white solid (43mg, 49%, >20:1 dr, crude NMR shows the same diastereoselectivity). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 3.53 (dd, *J* = 9.4, 3.3 Hz, 1H), 3.14 (dd, *J* = 12.1, 9.4 Hz, 1H), 2.61 – 2.50 (m, 2H), 2.20 – 2.10 (m, 2H), 2.04 – 1.94 (m, 2H), 1.81 – 1.70 (m, 1H), 1.69 – 1.57 (m, 1H), 1.48 – 1.40 (m, 2H), 1.43 – 1.32 (m, 1H), 1.26 (s, 6H) , 1.26 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.13, 128.30, 128.22, 125.64, 83.30, 53.97, 41.19, 36.08, 33.90, 25.11, 24.82, 21.83, 11.61; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.88; IR (neat): 2976.5 (m), 2956.3 (m), 2932.3 (m), 2867.2 (w), 1454.1 (w), 1380.7 (m), 1345.3 (m), 1210.3 (w), 1142.4 (s), 966.8 (w), 854.2 (w), 755.1 (m), 698.4 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{20}{}^{1}H_{31}{}^{11}B_{1}{}^{127}I_{1}{}^{16}O_{2}$ $[M+H]^+$: calculated: 441.1462, found: 441.1478. The relative stereochemistry was assigned by X-ray crystallography.





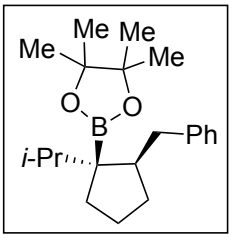
2-((1*R*,2*S*)-1-benzyl-2-methylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.11). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **3.1** (85.2 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). The crude reaction mixture was purified on silica gel

(hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a colorless oil (39.2 mg, 65%, > 20:1 dr, crude NMR shows the same diastereoselectivity). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.27 – 7.18 (m, 4H), 7.17 – 7.10 (m, 1H), 2.97 (d, *J* = 13.2 Hz, 1H), 2.43 (d, *J* = 13.3 Hz, 1H), 1.87 – 1.79 (m, 2H), 1.75 – 1.50 (m, 3H), 1.47 – 1.36 (m, 1H), 1.30 – 1.20 (m, 1H), 1.19 (s, 6H), 1.14 (s, 6H), 1.05 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.15, 130.14, 127.56, 125.49, 82.91, 44.35, 42.89, 33.97, 33.77, 25.14, 24.93, 22.24, 17.55; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.88; IR (neat): 2976.8 (m), 2953.6 (m), 2930.1 (m), 2869.0 (w), 1453.4 (w), 1387.9 (m), 1298.8 (m), 1211.8 (w), 1143.0 (s), 965.7 (w), 858.5 (w), 758.5 (w), 701.1 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{19}{}^{1}H_{29}{}^{11}B_{1}{}^{16}O_2$ $[M+H]^+$: calculated: 301.2339, found: 301.2336.



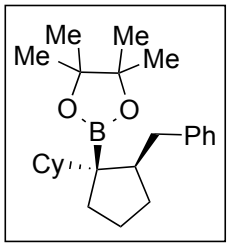
(3-((1*R*,2*R*)-2-benzyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)propoxy)(*tert*-butyl)dimethylsilane (3.17). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **S3.1** (58.5 mg, 0.1 mmol), KO*t*-Bu (22.4 mg, 0.2 mmol) and THF (0.5 mL). The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a white solid (30 mg, 65%, > 20:1 dr, crude NMR shows the same diastereoselectivity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 2H), 7.18 – 7.13 (m, 3H), 3.67 – 3.54 (m, 2H), 2.98 (dd, *J* = 13.2, 3.3 Hz, 1H), 2.33 (dd, *J* = 13.2, 11.6 Hz, 1H), 1.98 (ddd, *J* = 12.5, 8.7, 4.8 Hz, 1H),

1.82 – 1.43 (m, 7H), 1.35 – 1.21 (m, 2H), 1.27 (s, 12H), 1.21 – 1.06 (m, 1H), 0.91 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.00, 128.80, 128.07, 125.41, 82.93, 64.26, 53.02, 39.37, 34.41, 34.35, 31.36, 30.94, 26.02, 25.12, 24.89, 22.41, 18.40, -5.17; ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.27; IR (neat): 2975.9 (w), 2951.9 (m), 2929.1 (m), 2856.3 (m), 1453.9 (w), 1386.9 (m), 1299.6 (m), 1253.8 (m), 1215.5 (w), 1142.3 (s), 1098.6 (m), 990.1 (w), 835.3 (s), 775.1 (m), 698.6 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{27}{}^{1}H_{48}{}^{11}B_{1}{}^{16}O_{3}{}^{28}Si_{1}$ $[M+H]^+$: calculated: 459.3466, found: 459.3454.

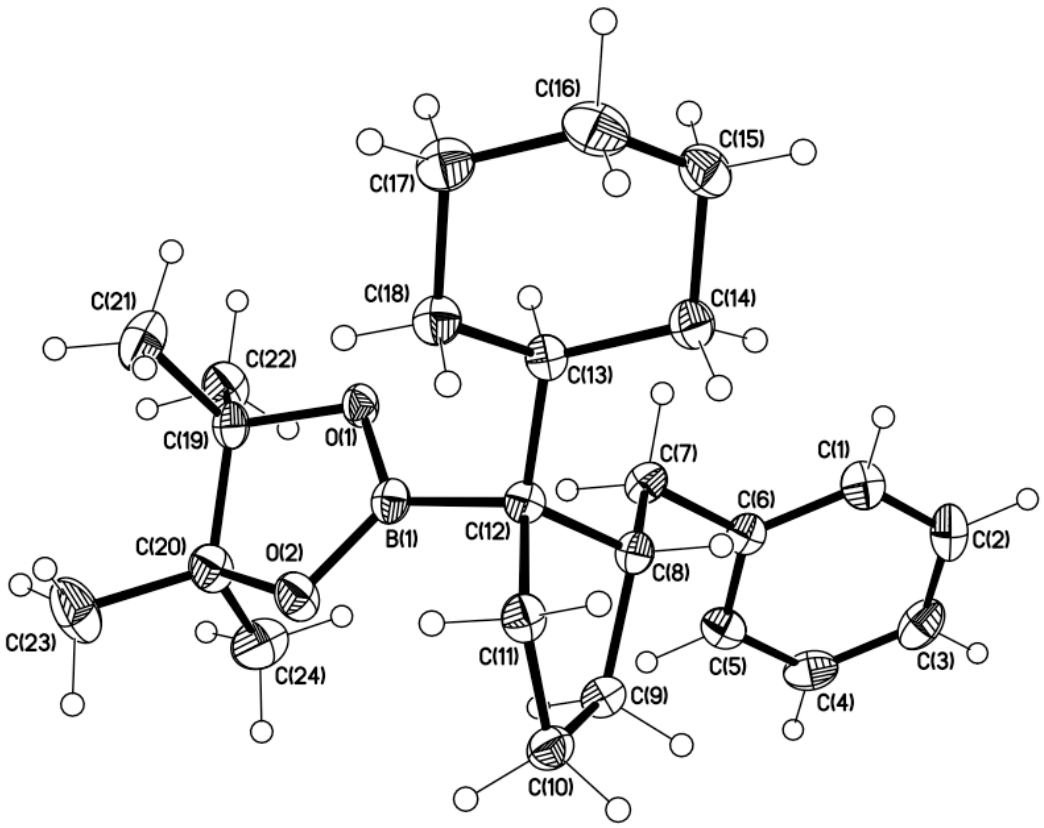


2-((1*R*, 2*R*)-2-benzyl-1-isopropylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.18). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **S3.2** (90.9 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a white solid (34.5 mg, 52.5%, > 20:1 dr, crude NMR shows the same diastereoselectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 – 7.22 (m, 2H), 7.19 – 7.12 (m, *J* = 6.9, 5.7, 1.4 Hz, 3H), 2.97 (dd, *J* = 13.2, 3.1 Hz, 1H), 2.34 (dd, *J* = 13.3, 11.7 Hz, 1H), 2.02 – 1.75 (m, 3H), 1.74 – 1.61 (m, 1H), 1.64 – 1.52 (m, 1H), 1.45 – 1.32 (m, 2H), 1.28 (s, 12H), 1.28 – 1.18 (m, 1H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.29, 128.77, 128.07, 125.39, 82.83, 48.45, 39.32, 31.82, 31.14, 29.17, 25.19, 24.93, 22.49, 21.15, 17.15; ^{11}B NMR

(160 MHz, $CDCl_3$) δ 34.37; IR (neat): 2955.3 (m), 2870.1 (w), 1495.1 (w), 1380.1 (m), 1297.7 (m), 1212.7 (w), 1140.6 (s), 982.1 (w), 864.9 (w), 745.6 (w), 699.2 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{21}{}^{1}H_{34}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^+$: calculated: 329.2652, found: 329.2655.



2-((1*R*,2*R*)-2-benzyl-1-cyclohexylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.16). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **S3.3** (98.9 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a white solid (59 mg, 80%, > 20:1 dr, crude NMR shows the same diastereoselectivity). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34 – 7.21 (m, 2H), 7.21 – 7.12 (m, 3H), 2.97 (dd, *J* = 13.3, 3.2 Hz, 1H), 2.34 (dd, *J* = 13.3, 11.9 Hz, 1H), 2.00 – 1.91 (m, 1H), 1.84 – 1.76 (m, 1H), 1.79 – 1.67 (m, 3H), 1.66 – 1.58 (m, 3H), 1.61 – 1.50 (m, 2H), 1.45 – 1.31 (m, 2H), 1.33 – 1.19 (m, 14H), 1.22 – 1.17 (m, 2H), 1.17 – 1.08 (m, 1H), 1.09 – 0.95 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.30, 128.78, 128.05, 125.36, 82.80, 47.14, 41.83, 39.18, 31.65, 31.56, 30.06, 27.34, 27.12, 27.08, 27.04, 25.22, 24.90, 22.39; ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.57; IR (neat): 2976.2 (m), 2925.3 (s), 2851.6 (m), 1449.0 (w), 1378.7 (m), 1297.3 (m), 1212.8 (w), 1141.8 (s), 864.2 (w), 746.5 (w), 698.8 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{24}{}^{1}H_{38}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^+$: calculated: 369.2965, found: 369.2967. The relative stereochemistry was assigned by X-ray crystallography.


C(16)
C(15)
C(17)
C(18)
C(14)
C(21)
C(22)
C(13)
C(19)
O(1)
C(7)
C(1)
C(6)
C(20)
O(2)
B(1)
C(12)
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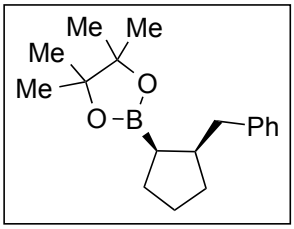
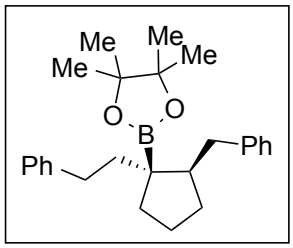
C(3)
C(24)
C(9)
C(4)
C(10)



2-((1*R*,2*R*)-2-benzylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.19). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **S3.4** (82.4 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a colorless oil (25.7 mg, 45%, > 18:1 dr, crude NMR shows the same diastereoselectivity). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 – 7.21 (m, 2H), 7.20 – 7.12 (m, 3H), 2.78 (dd, *J* = 13.4, 5.9 Hz, 1H), 2.51 (dd, *J* = 13.4, 8.6 Hz, 1H), 2.21 – 2.11 (m, 1H), 1.87 – 1.77 (m, 1H), 1.77 – 1.65 (m, 1H), 1.66 – 1.44 (m, 3H), 1.27 (d, *J* = 4.5 Hz, 1H), 1.18 (s, 6H), 1.17 (s, 6H), 0.99 – 0.86 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.22, 128.98, 128.05, 125.48, 82.72, 45.07, 42.49, 33.51, 28.47, 25.84, 24.72, 24.70; IR (neat): 2956.1 (s), 2932.8 (m), 2919.8 (m), 2876.6 (w), 2861.0 (w), 2361.0 (m), 2163.9 (s), 2013.9 (w), 1728.4 (s), 1379.0 (m), 1290.6 (s), 1316.8 (m), 1145.8 (m), 763.7 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{18}{}^{1}H_{27}{}^{11}B_{1}{}^{16}O_2$ $[M+H]^+$: calculated: 287.2182, found: 287.2194. Relative configuration was determined after oxidation and comparison with reported data.[80] To a 20 mL vial containing

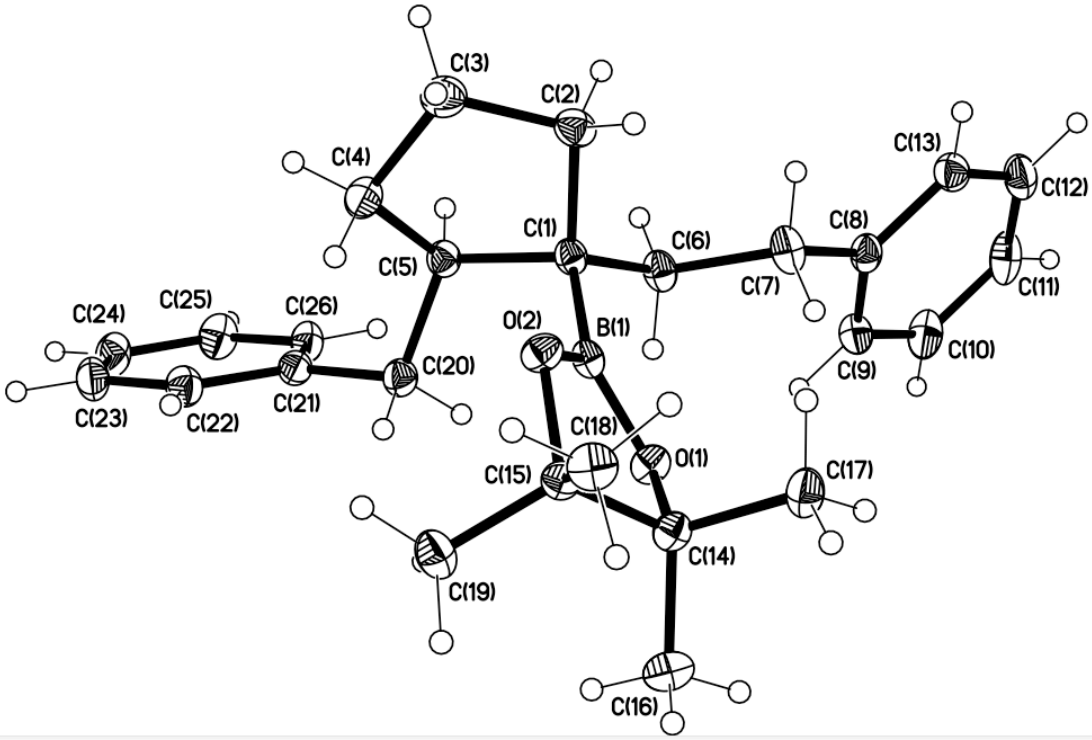
[80] Simpson, A. F.; Bodkin, C. D.; Butts, C. P.; Armitage, M. A.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3047-3054.

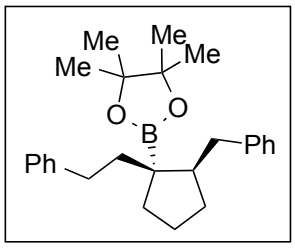
2-((1*R*,2*R*)-2-benzylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (10 mg, 0.035mmol), NaOH solution (3M, 1 mL) is added followed by THF (1 mL). The vial is then cooled to 0°C and H_2O_2 (30 wt%, 1 mL) is carefully added. The reaction mixture is then allowed to stir at room temperature for three hours, at which point, the mixture is cooled back to 0°C and saturated, aqueous $Na_2S_2O_3$ (1 mL) is added to degrade excess H_2O_2. The mixture is then extracted with ethyl acetate three times and the combined organics dried over Na_2SO_4, and concentrated *in vacuo*. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.27 (m, 2H), 7.22 – 7.17 (m, 3H), 3.96 – 3.87 (m, 1H), 2.76 (dd, *J* = 13.6, 6.9 Hz, 1H), 2.55 (dd, *J* = 13.6, 8.2 Hz, 1H), 2.08 – 2.00 (m, 1H), 1.99 – 1.92 (m, 1H), 1.89 – 1.80 (m, 1H), 1.77 – 1.66 (m, 1H), 1.66 – 1.54 (m, 2H), 1.34 – 1.25 (m, 1H), 1.23 (d, *J* = 4.1 Hz, 1H) ; ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.27.



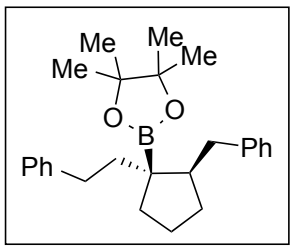
2-((1*R*,2*R*)-2-benzyl-1-phenethylcyclopentyl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane (3.14, major diastereomer). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **3.55** (103.3 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a white solid (52.7 mg, 67%, 4:1 dr, crude NMR shows the same diastereoselectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.12 (m, 10H), 3.01 (dd, *J* = 13.2, 3.3 Hz, 1H), 2.62 (ddd, *J* = 10.4, 5.8, 3.5 Hz, 2H), 2.36 (dd,

J = 13.2, 11.6 Hz, 1H), 2.20 – 2.04 (m, 2H), 1.81 – 1.47 (m, 5H), 1.46 – 1.31 (m, 2H), 1.31 (s, 6H), 1.31 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.76, 142.91, 128.80, 128.34, 128.25, 128.09, 125.50, 125.44, 83.07, 53.06, 41.31, 39.41, 34.42, 34.17, 31.42, 25.28, 24.89, 22.49; ; IR (neat): 2976.2 (m), 2930.8 (m), 2857.6 (w), 1495.3 (w), 1453.6 (m), 1386.7 (m), 1344.8 (w), 1300.7 (m), 1213.8 (m), 1141.2 (s), 1029.5 (w), 967.3 (w), 855.4 (w), 746.9 (m), 697.9 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{26}{}^{1}H_{39}{}^{11}B_{1}{}^{14}N_{1}{}^{16}O_{2}$ $[M+NH_4]^+$: calculated: 408.3074, found: 408.3091. The relative stereochemistry was assigned by X-ray crystallography.



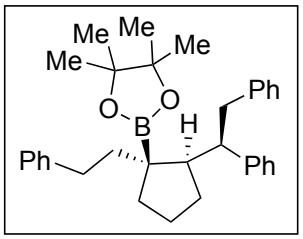


2-((1*S*,2*R*)-2-benzyl-1-phenethylcyclopentyl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane (3.14, minor diastereomer). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 (t, *J* = 7.6 Hz, 2H), 7.29 – 7.16 (m, 4H), 7.19 – 7.07 (m, 4H), 2.96 (dd, *J* = 13.1, 3.3 Hz, 1H), 2.63 – 2.55 (m, 2H), 2.29 (dd, *J* = 13.1, 11.8 Hz, 1H), 2.18 – 2.10 (m, 1H), 1.87 (ddd, *J* = 13.3, 10.4, 6.4 Hz, 2H), 1.74 – 1.64 (m, 2H), 1.61 – 1.44 (m, 3H), 1.38 – 1.27 (m, 1H), 1.31 (s, 6H), 1.31 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 143.80, 142.83, 128.81, 128.38, 128.28, 128.11, 125.55, 125.42, 83.05, 48.64, 36.78, 34.07, 33.33, 32.55, 29.80, 24.99, 24.71, 22.71; IR (neat): 2957.0 (s), 2930.9 (s), 2863.3 (m), 1728.6 (m), 1455.6 (w), 1376.6 (m), 1272.7 (m), 1142.1 (s), 1072.5 (w), 747.1 (w), 699.6 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{26}{}^{1}H_{39}{}^{11}B_{1}{}^{14}N_{1}{}^{16}O_{2}$ $[M+NH_4]^+$: calculated: 408.3074, found: 408.3079.



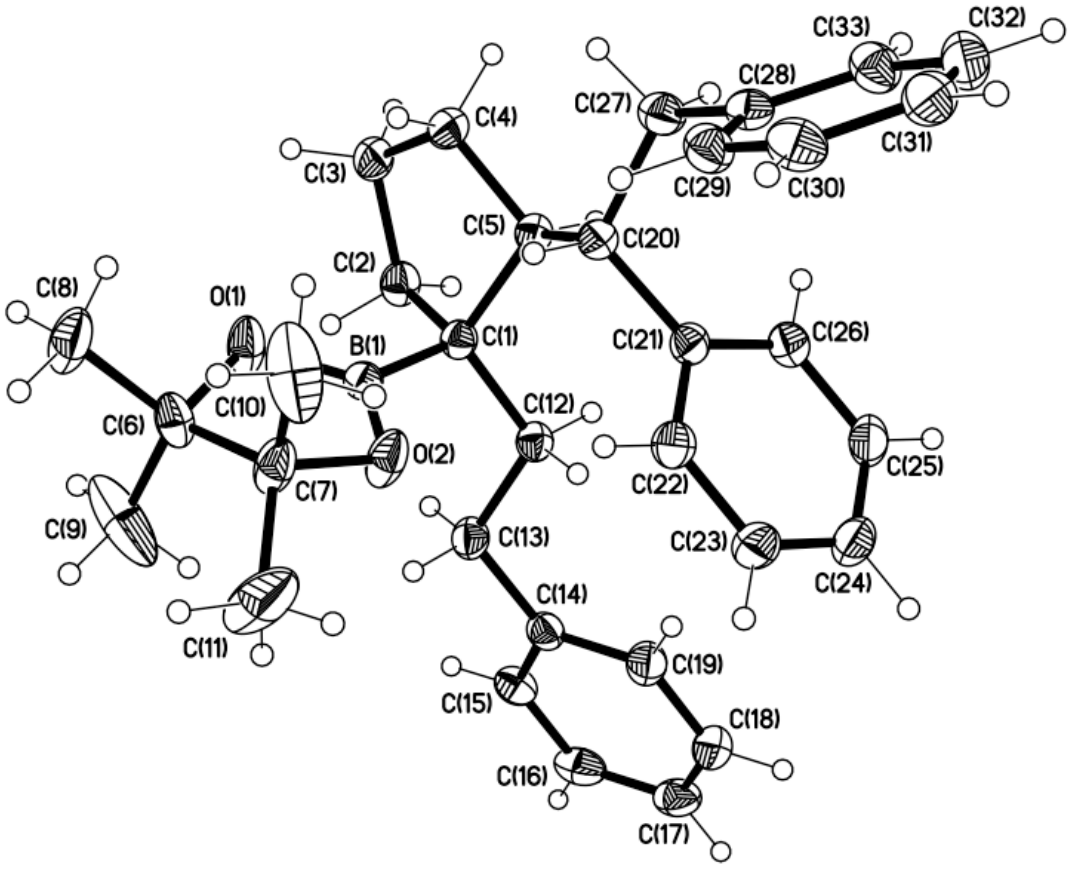
2-((1*R*,2*R*)-2-benzyl-1-phenethylcyclopentyl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane (3.14, major diastereomer). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **3.20** (103.3 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain

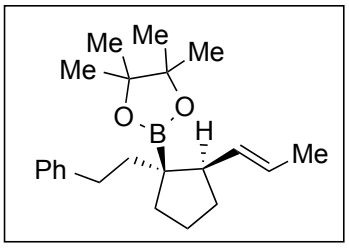
in CAM) to afford the desired product as a white solid (53.5 mg, 68%, 4:1 dr, crude NMR shows the same diastereoselectivity). The spectra is the same as above.



2-((1*R*,2*R*)-2-((*R*)-1,2-diphenylethyl)-1-phenethylcyclopentyl)-4,5,5,5-tetramethyl-1,3,2-dioxaborolane (3.15). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with 1,1-diboronate ester **3.55** (103.2 mg, 0.2 mmol), KO*t*-Bu (44.8 mg, 0.4 mmol) and THF (1 mL). Upon completion, the reaction mixture is quenched with benzyl bromide (171 mg, 1.0 mmol) and allowed to stir for an additional two hours. Mixture is then diluted with diethyl ether (2 mL) and filtered through a silica gel plug, rinsing with diethyl ether, and concentrated *in vacuo*. The crude residue is then purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a white solid (64 mg, 66 %, > 6:1 dr) with unresolved protonated byproduct. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14 (t, *J* = 7.5 Hz, 2H), 7.12 – 6.98 (m, 9H), 6.86 (d, *J* = 7.6 Hz, 4H), 3.19 (dd, *J* = 13.1, 3.7 Hz, 1H), 3.13 (ddd, *J* = 12.1, 8.6, 3.8 Hz, 1H), 2.69 (dd, *J* = 13.2, 11.6 Hz, 1H), 2.40 (td, *J* = 13.2, 4.5 Hz, 1H), 2.37 – 2.29 (m, 1H), 2.17 – 2.07 (m, 1H), 2.00 (ddd, *J* = 12.5, 8.4, 3.9 Hz, 2H), 1.84 – 1.67 (m, 2H), 1.68 – 1.57 (m, 1H), 1.45 – 1.33 (m, 1H), 1.32 – 1.24 (m, 1H), 1.27 (s, 6H), 1.27 (s, 6H), 0.84 (td, *J* = 12.9, 5.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 145.28, 143.65, 141.22, 129.02, 128.71, 128.36, 128.10, 127.86, 127.58, 127.53, 125.50, 125.12, 125.10, 82.77, 54.97, 50.49, 41.70, 39.54, 35.68, 32.64, 30.95, 25.33, 24.83, 21.93; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.49; IR (neat): 3026.1 (w), 2929.9 (m), 2859.7

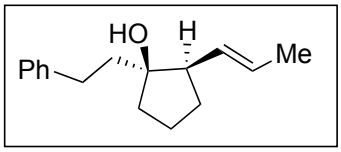
(w), 1728.7 (w), 1495.2 (w), 1453.2 (w), 1380.2 (m), 1141.5 (s), 967.6 (w), 862.8 (w), 746.1 (w), 697.9 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{33}{}^{1}H_{42}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 481.3278, found: 481.3291. The relative stereochemistry was assigned by X-ray crystallography.





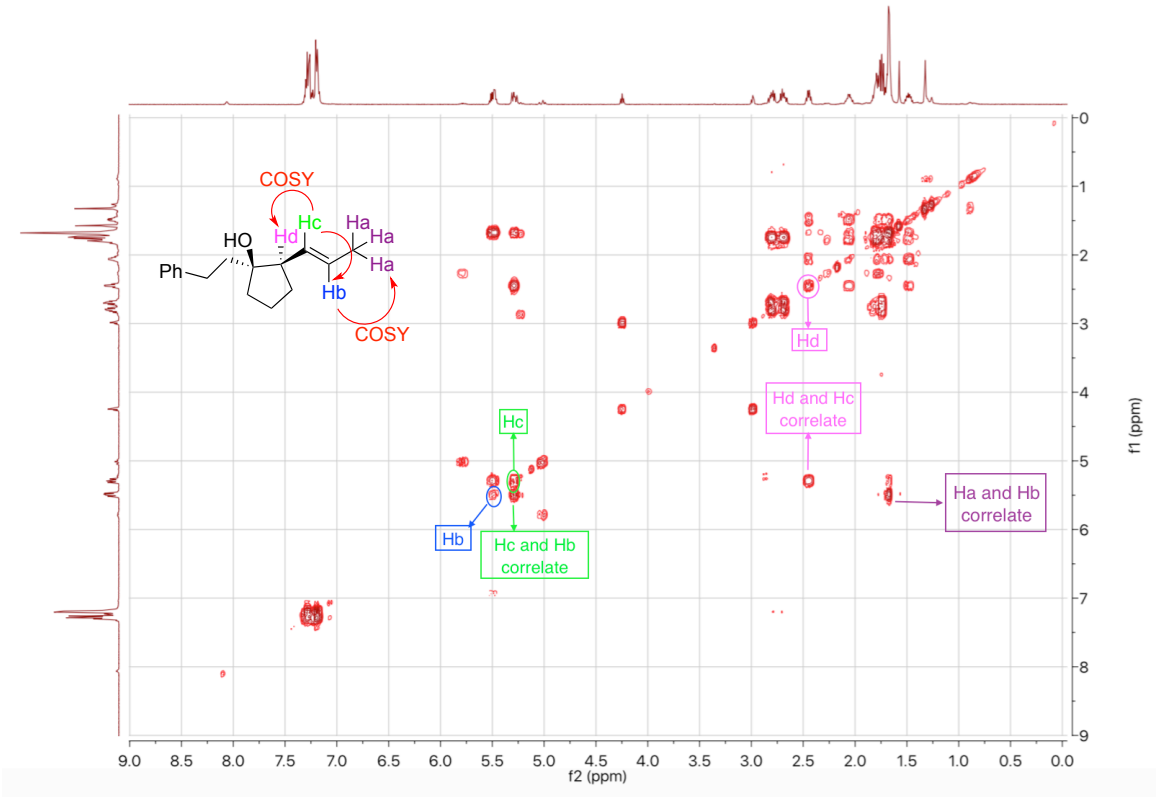
4,4,5,5-tetramethyl-2-((1*R*,2*R*)-1-phenethyl-2-((*E*)-prop-1-en-1-yl)cyclopentyl)-1,3,2-dioxaborolane (**3.23**). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with

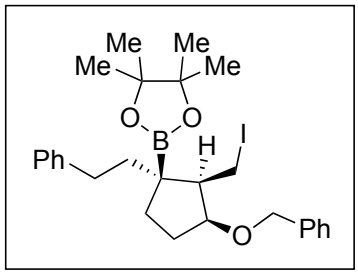
1,1-diboronate ester **3.22** (46.6 mg, 0.1 mmol), KO*t*-Bu (22.4 mg, 0.2 mmol) and THF (0.5 mL). Upon completion, the reaction mixture is diluted with diethyl ether (2 mL) and filtered through a silica gel plug, rinsing with diethyl ether, and concentrated *in vacuo*. The crude residue is then purified on silica gel (hexanes: diethyl ether = 100 : 1, stain in CAM) to afford the desired product as a colorless oil (18.8 mg, 55%, >20:1 dr, crude NMR shows the same diastereoselectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 – 7.22 (m, 2H), 7.21 – 7.13 (m, 3H), 5.52 – 5.35 (m, 2H), 2.57 (td, *J* = 12.8, 4.9 Hz, 2H), 2.47 (td, *J* = 12.9, 5.0 Hz, 1H), 1.99 – 1.82 (m, 1H), 1.80 – 1.66 (m, 3H), 1.65 (dd, *J* = 4.8, 0.7 Hz, 3H), 1.63 – 1.55 (m, 2H), 1.53 – 1.47 (m, 1H), 1.42 (td, *J* = 12.9, 5.0 Hz, 1H), 1.26 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.93, 132.52, 128.35, 128.16, 125.39, 124.38, 82.99, 49.25, 34.75, 34.01, 33.06, 31.09, 24.86, 24.71, 23.10, 18.08; ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.86; IR (neat): 2976.5 (m), 2955.3 (m), 2870.6 (m), 1726.8 (w), 1454.8 (w), 1379.3 (s), 1304.3 (m), 1272.9 (m), 1143.3 (s), 968.1 (w), 857.0 (w), 757.3 (s), 699.3 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{22}{}^{1}H_{34}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 341.2652, found: 341.2660.



(1*S*,2*R*)-1-phenethyl-2-((*E*)-prop-1-en-1-yl)cyclopentan-1-ol (**S3.7**). This reaction was performed to comfirm the structure of compound 4,4,5,5-tetramethyl-2-((1*R*,2*R*)-1-phenethyl-2-((*E*)-prop-1-en-1-yl)cyclopentyl)-1,3,2-dioxaborolane (**3.23**). To a 20 mL vial containing the compound (**3.23**) (25 mg, 0.0745

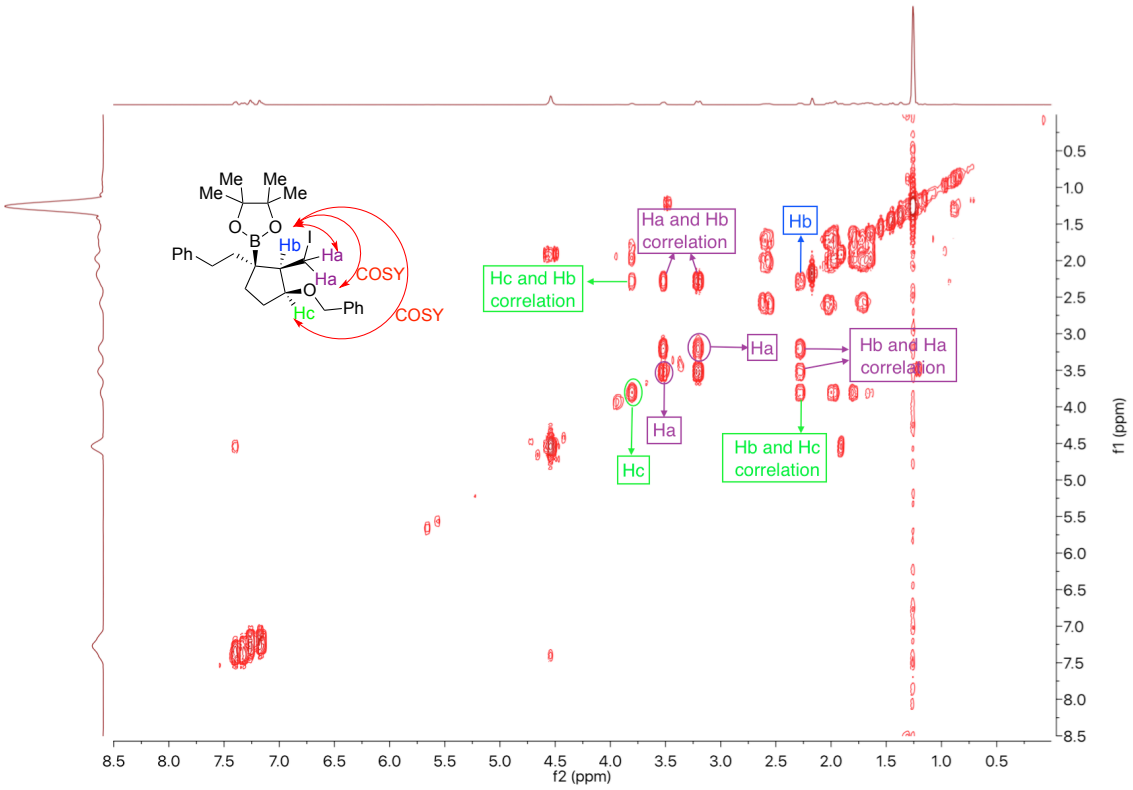
mmol) add THF (1 mL), NaOH (0.6 mL, 3 M, 1.8 mmol), then cool the vial to 0 °C. Add hydrogen peoxide (0.3 mL, 30% in H_2O) into the above mixture dropwise, let the reaction stir for overnight. The reaction was cooled to 0 °C again, and quenched by $Na_2S_2O_3$ (1 mL, saturated solution) slowly, stirred for 30 minutes, then extrated with diethyl ether, dried over Na_2SO_4, and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography (hexanes: ethyl acetate = 100 : 5 to 100 : 10, stain in CAM) on silica gel to afford desired product (11.8 mg, 70 % yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 5.49 (dqd, *J* = 15.1, 6.4, 0.9 Hz, 1H), 5.29 (ddq, *J* = 15.1, 9.2, 1.6 Hz, 1H), 2.80 (ddd, *J* = 13.4, 9.4, 7.5 Hz, 1H), 2.69 (ddd, *J* = 13.5, 9.6, 7.7 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.10 – 2.02 (m, 1H), 1.84 – 1.71 (m, 5H), 1.70 – 1.65 (m, overlap, 1H), 1.67 (dd, *J* = 6.4, 1.7 Hz, 3H), 1.53 – 1.45 (m, 1H), 1.32 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.99, 131.63, 128.88, 128.37, 125.96, 125.68, 83.62, 54.55, 39.24, 37.23, 30.28, 30.19, 21.02, 18.07. The structure was further confirmed by COSY spectra, shown below.

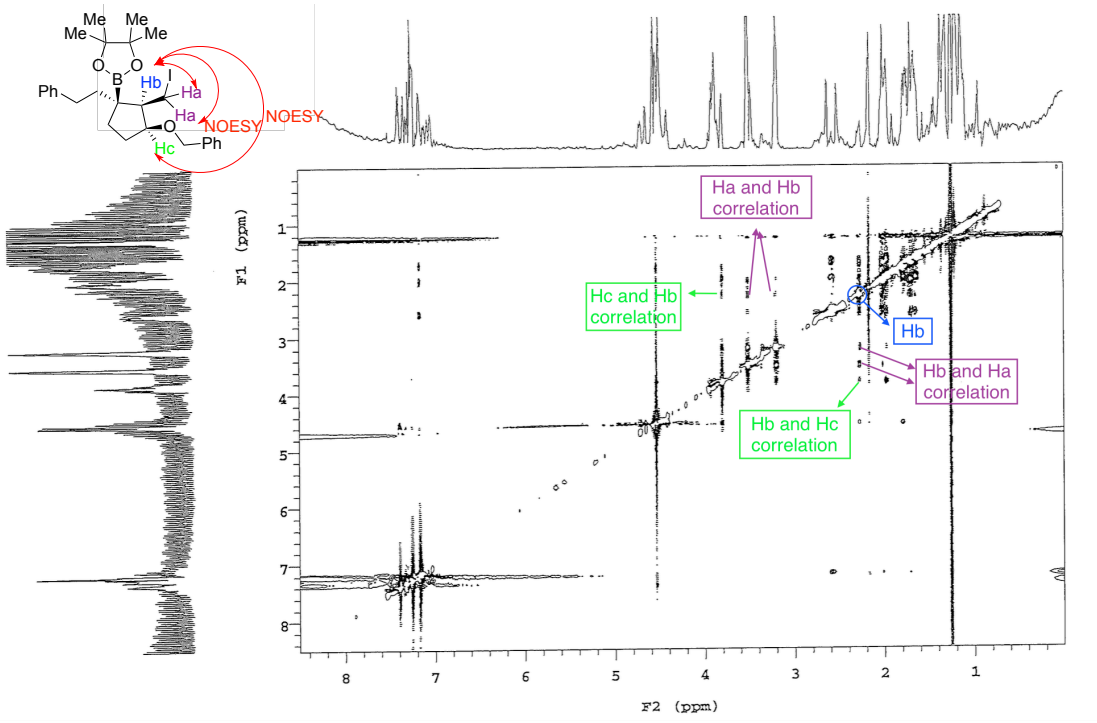


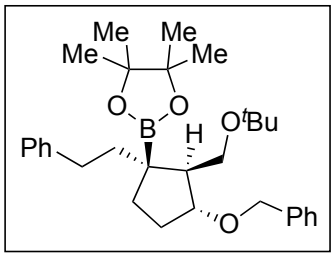


(1*S*,2*R*,3*S*)-2-(iodomethyl)-3-phenethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl benzoate (3.12, *major product*). The reaction was performed according to *Representative Procedure for Deborylative cyclization* with diboronate ester **S3.6** (55 mg, 0.1 mmol), KO*t*-Bu (22.4 mg, 0.20 mmol) and THF (0.5 mL) for overnight. Upon completion, the reaction mixture is quenched with a solution of I_2 (50.8 mg, 0.20 mmol) in anhydrous THF (0.3 mL) and allowed to stir at room temperature for three hours. Reaction mixture is then diluted with diethyl ether (2 mL) and filtered through a silica gel plug, rinsing with diethyl ether. Filtrate is then concentrated *in vacuo* and the crude residue purified by column chromatography on silica

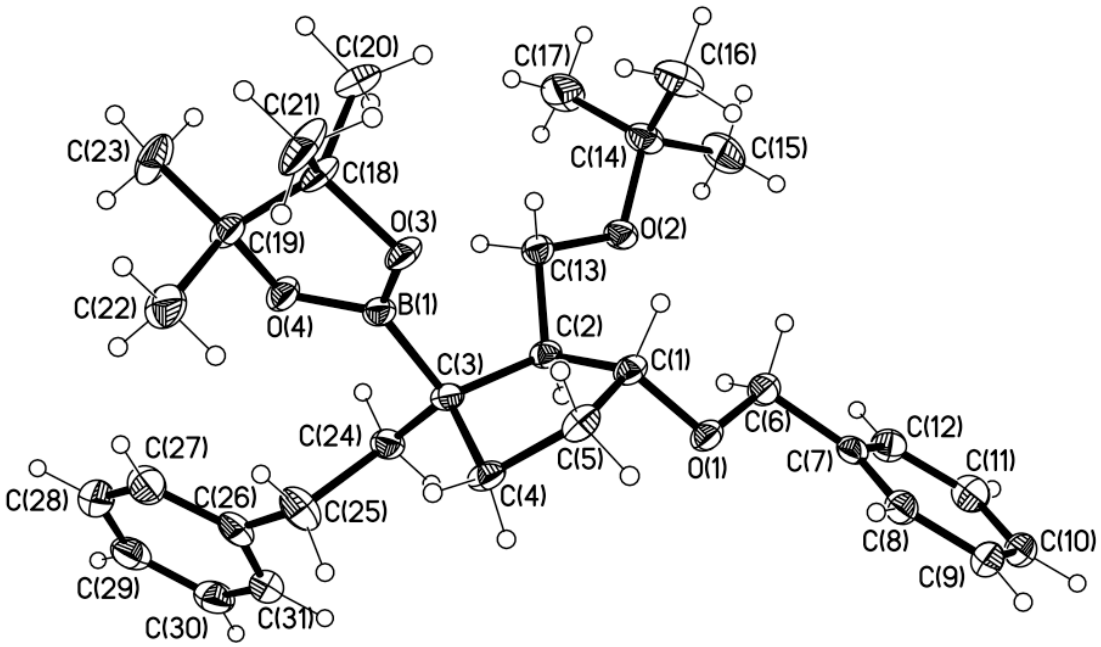
gel (100 : 0.8 Hexanes/EtOAc, gradient to 100 : 3 Hexanes/EtOAc, stain in CAM) to afford a colorless oil (29.3 mg, 55%, product **3.12** : product **S3.8** = 2.9 : 1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 – 7.38 (m, 2H), 7.36 – 7.30 (m, 2H), 7.29 – 7.24 (m, 3H), 7.20 – 7.14 (m, 3H), 4.55 (d, *J* = 1.9 Hz, 2H), 3.81 (qd, *J* = 4.6, 3.2 Hz, 1H), 3.52 (dd, *J* = 9.8, 4.8 Hz, 1H), 3.21 (t, *J* = 10.1 Hz, 1H), 2.67 – 2.50 (m, 2H), 2.28 (dt, *J* = 10.0, 4.8 Hz, 1H), 2.10 – 1.94 (m, 3H), 1.85 – 1.75 (m, 1H), 1.75 – 1.61 (m, 2H), 1.26 (two sets of singlet, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.05, 138.81, 128.30, 128.26, 128.24, 127.85, 127.36, 125.59, 87.16, 83.41, 71.26, 57.60, 41.33, 33.47, 33.27, 30.50, 25.07, 24.90, 8.22; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.39; IR (neat): 2975.4 (w), 2926.7 (w), 2855.7 (w), 1495.8 (w), 1378.8 (m), 1310.9 (m), 1198.9 (m), 1166.4 (s), 1140.4 (s), 1099.2 (m), 1066.9 (m), 856.9 (m), 735.0 (s), 697.3 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{27}{}^{1}H_{36}{}^{11}B_{1}{}^{16}O_{3}{}^{127}I_{1}{}^{23}Na_{1}$ $[M+Na]^{+}$: calculated: 569.1700, found: 569.1707. The relative stereochemistry was assigned by COSY and NOESY spectra, shown below.


Me
Me
Me
Me
O
O
B
Hb
Ha
Ha
O
Ph
Hc
Ph
COSY
COSY
Ha and Hb correlation
Hb
Hc and Hb correlation
Ha
Hb and Ha correlation
Ha
Hc
Hb and Hc correlation
f1 (ppm)
f2 (ppm)


Me
Me
Me
Me
O
O
B
Hb
Ha
Ha
O
Ph
Hc
Ph
NOESY
NOESY
Ha and Hb correlation
Hc and Hb correlation
Hb
Hb and Ha correlation
Hb and Hc correlation
F1 (ppm)
F2 (ppm)

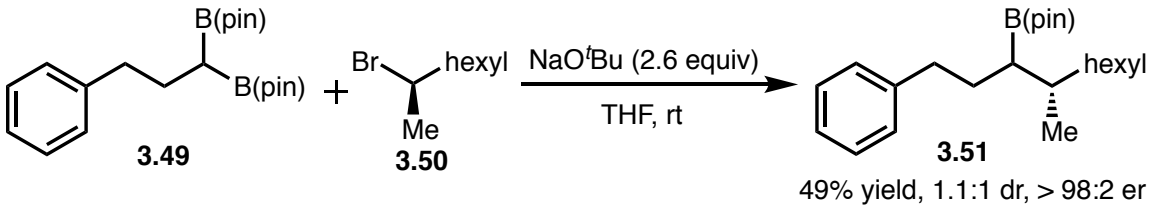


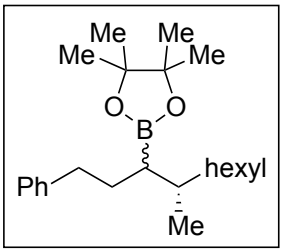
2-((1*S*,2*S*,3*R*)-3-(benzyloxy)-2-(*tert*-butoxymethyl)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (S3.8, *minor product*). This product was isolated along side the above product **(3.12)**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.33 (m, 2H), 7.33 – 7.28 (m, 2H), 7.28 – 7.22 (m, 3H), 7.21 – 7.17 (m, 2H), 7.17 – 7.13 (m, 1H), 4.57 (d, *J* = 12.3 Hz, 1H), 4.50 (d, *J* = 12.3 Hz, 1H), 3.82 (dt, *J* = 6.9, 3.5 Hz, 1H), 3.52 (dd, *J* = 8.8, 5.0 Hz, 1H), 3.18 (dd, *J* = 9.8, 8.8 Hz, 1H), 2.68 – 2.47 (m, 2H), 2.07 – 1.92 (m, 3H), 1.87 (ddd, *J* = 11.5, 7.1, 4.1 Hz, 1H), 1.83 – 1.67 (m, 2H), 1.63 (ddd, *J* = 11.9, 9.5, 7.4 Hz, 1H), 1.26 (s, 12H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.68, 139.66, 128.39, 128.17, 128.12, 127.59, 127.00, 125.38, 84.60, 82.99, 72.49, 70.49, 62.86, 56.23, 41.83, 33.73, 32.97, 31.65, 27.66, 25.11, 24.93; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.59; IR (neat): 3026.0 (w), 2972.8 (s), 2927.6 (m), 2857.0 (m), 1496.0 (m), 1378.4 (s), 1307.1 (m), 1198.5 (m), 1143.6 (s), 1073.9 (m), 857.5 (w), 698.5 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{31}{}^{1}H_{45}{}^{11}B_{1}{}^{16}O_{4}{}^{23}Na_{1}$ $[M+Na]^{+}$: calculated: 515.3309, found: 515.3320. The relative stereochemistry was assigned by X-ray crystallography, shown below:



3.7.7 Radical Probe Experiment I

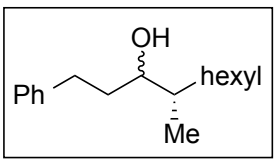
Procedure for Deborylative Alkylation Experiment:





4,4,5,5-tetramethyl-2-((4*S*)-4-methyl-1-phenyldecan-3-yl)-1,3,2-dioxaborolane (3.51). In the glove box, an oven-dried 2-dram vial equipped with magnetic stir bar is charged with 1,1-diboronate ester **3.49** (96.8 mg, 0.26 mmol), NaO^{t}Bu (50 mg,

0.52 mmol), and THF (1 mL). The reaction mixture was allowed to stir at room temperature for 15 min, followed by the addition of (*R*)-2-bromooctane (35.1 mL, 0.20 mmol). The vial was sealed with a polypropylene cap, removed from the glove box, and was allowed to stir at room temperature for overnight. Upon completion, the reaction mixture was diluted with diethyl ether (2 mL), filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100:1 to 50:1) to isolate the desired product (35 mg, 49%, 1.1:1 d.r. 98:2 er)(diastereoselectivity was determined based on NMR integration after oxidation). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28 – 7.26 (m, 3H), 7.21 – 7.13 (m, 2H), 2.72 – 2.57 (m, 1H), 2.57 – 2.43 (m, 1H), 1.87 – 1.68 (m, 1H), 1.68 – 1.56 (m, 2H), 1.43 – 1.33 (m, 1H), 1.32 – 1.19 (m, 8 H, overlap), 1.27 (s, 12H), 1.18 – 1.07 (m, 1H), 1.04 - 0.98 (m, 1H), 0.93 – 0.84 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.26, 128.36, 128.17, 125.48, 82.83, 36.42, 36.15, 36.09, 35.91, 34.62, 34.38, 31.89, 31.51, 30.20, 29.58, 29.56, 27.52, 27.25, 25.08, 25.06, 24.79, 22.64, 18.75, 18.44, 14.09; IR (neat): 2956.5 (m), 2926.9 (s), 2856.3 (m), 1729.6 (w), 1456.9 (w), 1379.1 (m), 1313.8 (m), 1270.7 (w), 1143.9 (s), 699.1 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{23}{}^{1}H_{40}{}^{11}B_{1}{}^{16}O_{2}$ $[M+H]^{+}$: calculated: 359.3121, found: 359.3139.

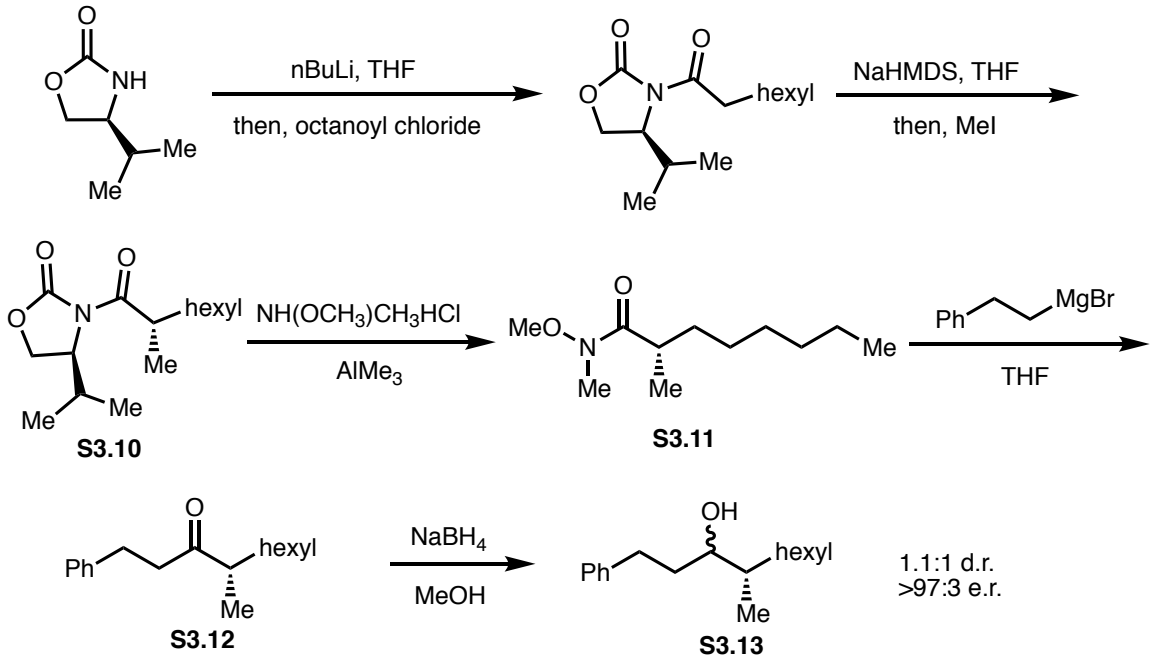


(4*S*)-4-methyl-1-phenyldecan-3-ol (S3.9). To a 20 mL vial containing the compound **3.51** and THF (1 mL), aqueous NaOH

(0.6 mL, 3 M, 1.8 mmol) is added then the vial is cooled 0 °C. Aqueous Hydrogen Peroxide (0.3 mL, 30% in H_2O) is then slowly added to the reaction vessel and reaciton allowed to stir overnight. Upon return, the vessel is cooled back to 0 °C and quenched slowly with saturated, aqueous $Na_2S_2O_3$ (1 mL), stirred for 30 minutes, then extrated with diethyl ether. Combined extracts are then dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue is then purified by column chromatography on silica gel. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 – 7.27 (m, 4H), 7.24 – 7.16 (m, 6H), 3.54 (dt, *J* = 10.6, 5.5 Hz, 1H), 3.48 (dtd, *J* = 9.8, 5.1, 2.9 Hz, 1H), 2.95 – 2.78 (m, 2H), 2.73 – 2.59 (m, 2H), 1.84 – 1.73 (m, 4H), 1.57 – 1.47 (m, 2H), 1.46 – 1.38 (m, 2H), 1.38 – 1.22 (m, 17H), 1.21 –1.14 (m, 2H), 1.14 – 1.05 (m, 1H), 0.95 – 0.84 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 142.36, 142.31, 128.42, 128.36, 125.76, 75.44, 74.72, 39.01, 38.45, 36.26, 35.19, 33.23, 32.69, 32.56, 31.92, 31.84, 29.69, 29.60, 29.58, 27.31, 27.25, 22.65, 15.20, 14.08, 13.69; IR (neat): 3357.0 (w), 2956.7 (m), 2927.8 (s), 2855.0 (m), 1724.7 (m), 1455.3 (w), 1275.3 (w), 1131.9 (w), 751.2 (m), 698.4 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{17}{}^1H_{27}$ $[M+H-H_2O]^+$: calculated: 231.2113, found: 231.2118.

Proof of Stereochemistry:

The same title compound was prepared from Evans Alkylation as shown below:



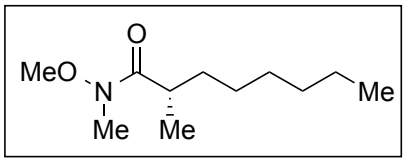
(*R*)-4-isopropyl-3-((*S*)-2-methyloctanoyl)oxazolidin-2-one **(S3.10)** prepared according to the literature procedure.[81] The product is obtained as a colorless oil (78%, d.r. = 88:12). The NMR spectra are in accord with previously reported data.[82] Preparation of (*S*)-*N*-methoxy-*N*,2-dimethyloctanamide **S3.11** adapted from literature procedure.[83] To a stirred solution of *N*,*O*-Dimethylhydroxylamine hydrochloride (312.1 mg, 3.2 mmol) in CH_2Cl_2 (5 ml) at 0 °C, neat $AlMe_3$ (307 mL, 3.2 mmol) is carefully added. The

[81] Evans, D. A.; Ennis, M. D.; Le, T.; Mandel, N.; Mandel, G. *J. Am. Chem. Soc.* **1984**, *106*, 1154-1156.

[82] Minko, Y.; Pasco, M.; Lercher, L.; Botoshansky, M.; Marek, I. *Nature* **2012**, *490*, 522-526.

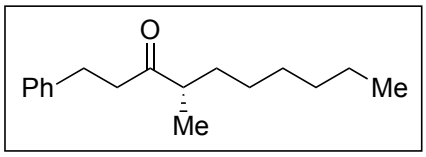
[83] Micalizio, G. C.; Pinchuk, A. N.; Roush, W. R. *J. Org. Chem.* **2000**, *65*, 8730-8736.

reaction mixture is stirred at 0 °C for 10 min and then one hour at room temperature. The mixture is then cooled back to 0 °C and a solution of oxazolidone **S3.10** (227 mg, 0.8 mmol) in CH_2Cl_2 (5 ml) is added to the reaction vessel. The resulting mixture is then allowed to stir overnight, gradually reaching room temperature. Upon return, the reaction solution is diluted with CH_2Cl_2 (10 mL) and poured into a separatory funnel containing ice-cold aqueous 0.5 N HCl (25 ml) and organics are extracted 3x with CH_2Cl_2. The combined extracts are then washed with saturated, aqueous $NaHCO_3$ and saturated, aqueous NaCl, in succession, then dried over Na_2SO_4. Volatiles are then removed *in vacuo* and the crude, colorless oil is then purified by silica gel chromatography (8:2 pentane/Et_2O, gradient to 7:3 pentane/Et_2O) to afford (*S*)-*N*-methoxy-*N*,2-dimethyloctanamide **S3.11** as a colorless oil (38.2 mg, 22 %).



(*S*)-*N*-methoxy-*N*,2-dimethyloctanamide (S3.11). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.68 (s, 3H), 3.19 (s, 3H), 2.86 (s, 1H), 1.67 (ddd, *J* = 13.2, 8.3, 5.3 Hz, 1H), 1.32 – 1.18 (m, 9H), 1.11 (d, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 61.40, 35.09, 33.83, 31.73, 29.68, 29.31, 27.50, 22.61, 17.45, 14.04; IR (neat): 2964.0 (m), 2930.4 (m), 2871.7 (m), 1779.3 (s), 1699.3 (m), 1385.5 (m), 1300.8 (w), 1204.9 (m), 1141.6 (m), 911.6 (w), 733.4 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{11}{}^{1}H_{24}{}^{14}N_1{}^{16}O_2$ $[M+H]^+$: calculated: 202.1807, found: 202.1797.

To a dried flask fitted with magnetic stir bar and charged with Mg^0 (36.5 mg, 1.5 mmol) and anhydrous THF (5 mL), (2-bromoethyl)benzene (0.17 mL, 1.25 mmol) is added slowly under N_2. Mixture is then stirred at 60 °C for two hours and the resulting Grignard solution is cooled back to room temperature where it is added to a solution of amide **S3.11** (38.2 mg, 0.177 mmol) in anhydrous THF (1 mL) drop wise at 0 °C. The reaction mixture is allowed to stir for 3h, gradually warming to room temperature. Upon completion, reaction is cooled to 0 °C and quenched with saturated, aqueous NH_4Cl (1 mL). Organics are then extracted with diethyl ether (3 × 3 mL) and the combined extracts washed with brine and dried over anhydrous Na_2SO_4. Volatiles are then removed *in vacuo* and the crude residue was purified on silica gel (hexane: ethyl acetate= 100:1, gradient to 20:1) to afford compound **S3.12** as colorless oil (34 mg, 78%).



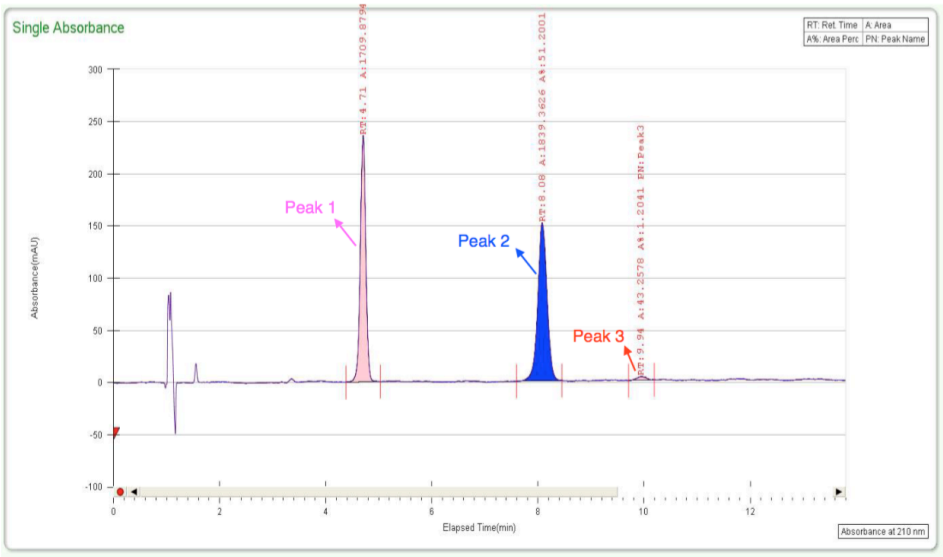
(*S*)-4-methyl-1-phenyldecan-3-one (S3.12). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.26 (m, 2H), 7.21 – 7.16 (m, 3H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.78 – 2.70 (m, 2H), 2.48 (h, *J* = 6.9 Hz, 1H), 1.65 – 1.56 (m, 1H), 1.35 – 1.12 (m, 9H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.81, 141.35, 128.41, 128.33, 126.00, 46.54, 42.65, 32.94, 31.63, 29.74, 29.30, 27.18, 22.56, 16.16, 14.03; IR (neat): 2958.0 (s), 2928.3 (s), 2858.2 (m), 1728.0 (s), 1462.1 (m), 1272.6 (s), 1122.5 (m), 1072.6 (m), 744.7 (w), 699.4 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{17}{}^{1}H_{27}{}^{16}O_1$ $[M+H]^+$: calculated: 247.2062, found: 247.2053.

To a vial containing a solution of (*S*)-4-methyl-1-phenyldecan-3-one **S3.12** (34 mg, 0.14 mmol) in MeOH (1 mL), $NaBH_4$ (10.6 mg, 0.28 mmol) is added at 0 °C. The reaction mixture is then allowed to stir for 20 min at room temperature, then quenched with saturated aqueous NH_4Cl (1 mL). Organics are then extracted with diethyl ether (3 × 3 mL) and the combined organic layers washed with brine and dried over anhydrous Na_2SO_4. Volatiles are then removed *in vacuo* and the crude residue purified on silica gel (hexane: ethyl acetate = 10:1) to yield (4*S*)-4-methyl-1-phenyldecan-3-ol **S3.13** as an colorless oil (32 mg, 92%, 1.1:1 d.r., 97:3 er). (diastereoselectivity was determined based on NMR integration). The spectra data is the same as shown above.

Analysis of Stereochemistry

The enantioselectivity was determined by SFC analysis of the reaction product shown below.

SFC trace of base promoted deborylative alkylation product compound **30** (after oxidation):



General Info	
Log Author	
Log Date	9/13/2015 6:29:58 PM
Report By	current_User
Report Date	4/10/2017
Method Name	potterbo.met
Notes	OD-H, 100 bar, 10% IPA, 3 mL/min, 35 deg C

Injection Info			
Inj Vol	10	Temp	34.8
Solvent	IPA	Flow	3
Column	OD-H	% Modifier	10
Sample	xl-4-098-fineagain	Pressure	100
Well location	P1: 1A		

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	47.5958	1709.8794	4.71	236.3671	0.0042
2	51.2001	1839.3626	8.08	151.5557	0.0073
3	1.2041	43.2578	9.94	3.6284	0.009
Total:	100	3592.4998			

Diastereoselectivity = Area of Peak1/ Area of (Peak 2 + Peak 3)

= 1709.8794/ (1839.3626 + 43.2578)

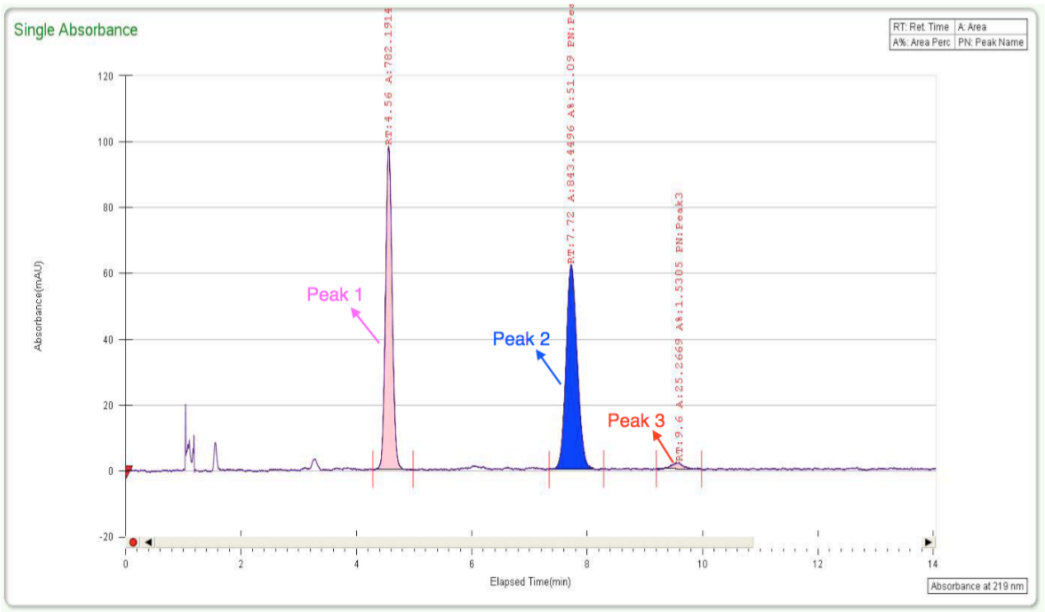
= 1/1.1

Enantioselectivity = Area of (Peak 2 - Peak 3)/ Area of (Peak 2 + Peak 3)

= (1839.3626 - 43.2578)/ (1839.3626 + 43.2578)

= 95 %

SFC trace of authentic product prepared from Evans alkylation compound **S19**:



General Info	
Log Author	
Log Date	10/19/2015 5:12:06 PM
Report By	current_User
Report Date	4/10/2017
Method Name	potterbo.met
Notes	ODH, 100 bar, 10% iPA, 3 mL/min, 35 deg C

Injection Info	
Inj Vol	10
Solvent	IPA
Column	OD-H
Sample	xl-4-271-finediluteagain
Well location	P1: 3A
Temp	35
Flow	3
% Modifier	10
Pressure	101

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	47.3795	782.1914	4.56	97.939	0.0044
2	51.09	843.4496	7.72	62.1709	0.0075
3	1.5305	25.2669	9.6	1.8841	0.0093
Total:	100	1650.9079			

Diastereoselectivity = Area of Peak1/ Area of (Peak 2 + Peak 3)

= 782.1914/ (843.4496 + 25.2669)

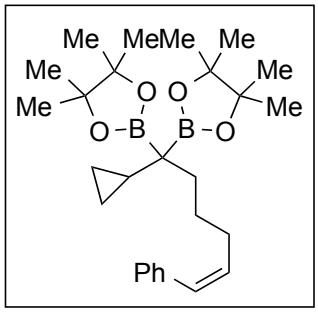
= 1/1.1

Enantioselectivity = Area of (Peak 2 - Peak 3)/ Area of (Peak 2 + Peak 3)

= (843.4496 - 25.2669)/ (843.4496 + 25.2669)

= 94 %

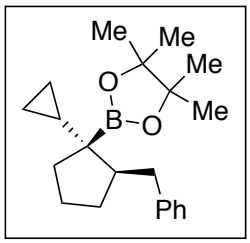
3.7.8 Radical Probe Experiment II



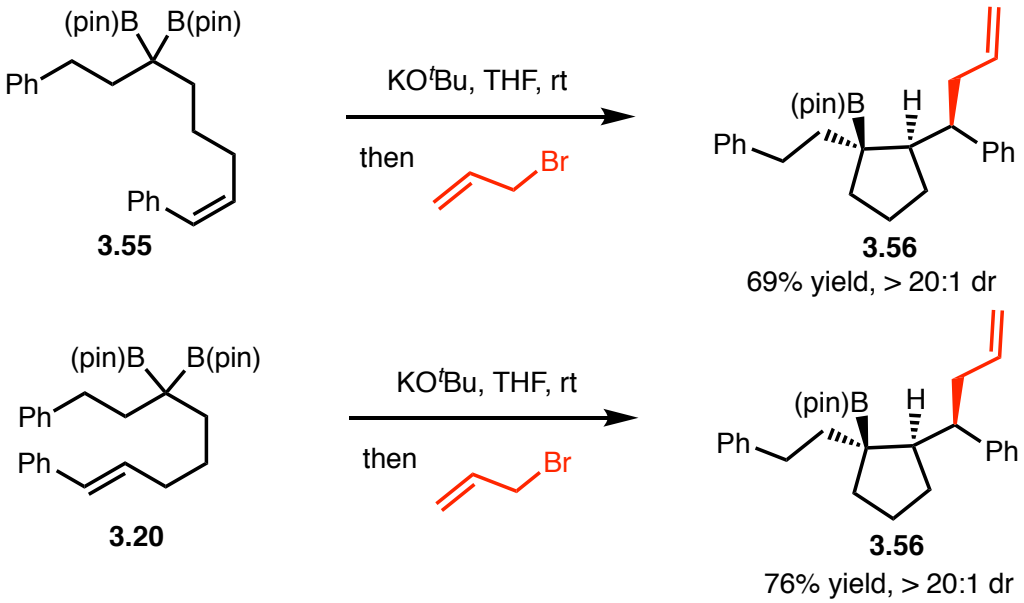
(*Z*)-2,2'-(1-cyclopropyl-6-phenylhex-5-ene-1,1-diyl)bis(4,4, 5,5-tetramethyl-1,3,2-dioxaborolane) (**3.39**). The reaction was performed according to *Representative Procedure (Method C)* with 2,2'-(cyclopropylmethylene) bis(4,4,5,5-tetramethyl-1,3,2- dioxaborolane) (154 mg, 0.5 mmol, made according to previous procedure [84]), LTMP (77.3 mg, 0.53 mmol), (*Z*)-(5-bromopent-1-en-1-yl)benzene (118.2 mg, 0.53mmol) and THF (2 mL). The crude reaction mixture was purified by column chromatography on silica gel (100:1 – 50:1 hexanes/ethyl acetate, stain in CAM) to afford a white solid (226 mg, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.24 (m, 4H), 7.25 – 7.17 (m, 1H), 6.38 (d, *J* = 11.7 Hz, 1H), 5.73 (dt, *J* = 11.5, 7.7 Hz, 1H), 2.35 (q, *J* = 7.0 Hz, 2H), 1.82 – 1.53 (m, 4H), 1.22 (s, 24H), 0.86 (tt, *J* = 8.1, 5.6 Hz, 1H), 0.49 – 0.28 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.92, 133.70, 128.76, 128.28, 128.02, 126.26, 82.76, 33.04, 29.80, 28.64, 24.72, 24.71, 12.93, 3.62; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.49; IR (neat): 2977.3 (m), 2931.1 (w), 1378.7 (m), 1342.2 (m), 1305.2 (s), 1268.1 (m), 1214.4 (w), 1137.5 (s), 853.5 (w), 699.2

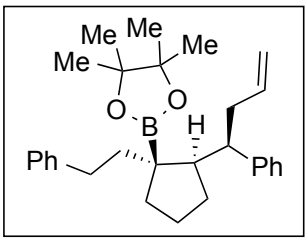
[84] K. Hong, X. Liu, and J. P. Morken *J. Am. Chem. Soc.* **2014**, *136,* 10581-10584.

(w) cm^{-1}; HRMS-(DART+) for $^{12}C_{30}{}^{1}H_{49}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: calculated: 495.3817, found: 495.3819.



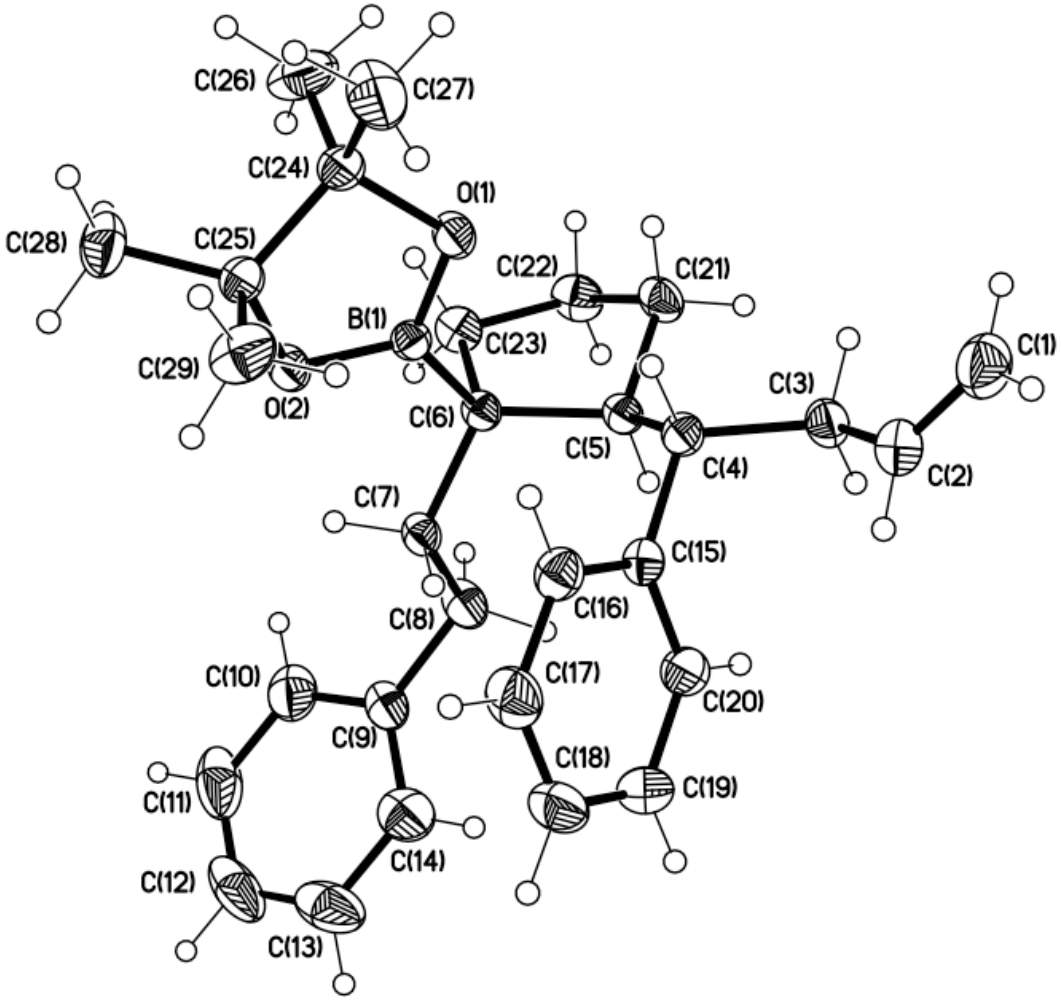
2-((1*R*,2*R*)-2-benzyl-1-cyclopropylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.40). The reaction was performed according to *Representative Procedure for Deborylative cyclization* with diboronate ester **3.39** (45.2 mg, 0.1 mmol), KO*t*-Bu (22.4 mg, 0.2 mmol), and THF (0.5 mL) for 6 hours. The crude reaction mixture was purified by column chromatography on silica gel (100:0.8 hexanes/ethyl acetate, stain in CAM) to afford a colorless oil (15 mg, 46 %, d.r. > 20:1, crude NMR shows the same diastereoselectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 – 7.22 (m, 2H), 7.24 – 7.12 (m, 3H), 3.07 (dd, J = 13.2, 3.5 Hz, 1H), 2.43 (dd, J = 13.2, 11.7 Hz, 1H), 1.87 (tdd, J = 9.0, 6.6, 3.5 Hz, 1H), 1.76 – 1.62 (m, 1H), 1.66 – 1.57 (m, 2H), 1.52 – 1.40 (m, 1H), 1.35 – 1.19 (m, 1H), 1.26 (s, 12H), 1.15 – 1.02 (m, 1H), 0.86 (ddt, J = 11.3, 8.6, 3.7 Hz, 1H), 0.44 – 0.26 (m, 1H), 0.29 – 0.16 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.17, 128.89, 128.04, 125.35, 82.84, 52.53, 39.16, 30.96, 30.57, 24.92, 24.83, 22.42, 16.75, 2.07, 0.29; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.78; IR (neat): 2976.4 (w), 2954.8 (w), 2866.4 (w), 1495.0 (w), 1387.8 (m), 1299.9 (m), 1214.2 (w), 1141.6 (s), 1013.6 (w), 967.5 (w), 862.4 (w), 744.8 (w), 699.3 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{21}{}^{1}H_{32}{}^{11}B_1{}^{16}O_2$ $[M+H]^+$: calculated: 327.2495, found: 327.2492.

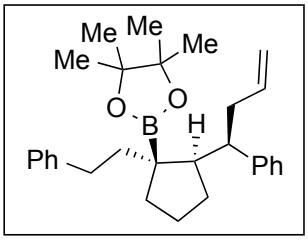




4,4,5,5-tetramethyl-2-((1*R*,2*R*)-1-phenethyl-2-((*R*)-1-phenylbut-3-en-1-yl)cyclopentyl)-1,3,2-dioxaborolane (3.56). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with (*Z*)-2,2'-(1,8-diphenyloct-7-ene-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **(3.55)** (56.13 mg, 0.1 mmol), KO*t*-Bu (22.4 mg, 0.2 mmol) and toluene (0.5 mL). Upon completion, the reaction mixture is quenched with allyl bromide (60.5 mg, 0.5 mmol) and allowed stir an additional two hours. Mixture then diluted with diethyl ether (2 mL) and filtered through a silica gel plug, rinsing with diethyl ether. Filtrate is then concentrated *in vacuo* and the crude residue purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a white solid (30.7 mg, 69%, >10:1 dr, crude NMR shows the same diastereoselectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 –

7.18 (m, 4H), 7.19 – 7.11 (m, 3H), 7.14 – 7.04 (m, 1H), 6.91 – 6.85 (m, 2H), 5.50 (dddd, J = 18.0, 10.0, 7.4, 6.0 Hz, 1H), 4.85 (dd, J = 17.1, 1.7 Hz, 1H), 4.81 – 4.76 (d, J = 10.0, 1H), 2.92 (td, J = 10.2, 8.8, 3.7 Hz, 1H), 2.59 – 2.47 (m, 1H), 2.40 (td, J = 13.2, 4.5 Hz, 1H), 2.36 – 2.25 (m, 2H), 1.97 (td, J = 8.9, 8.4, 4.8 Hz, 2H), 1.87 (q, J = 8.7 Hz, 1H), 1.73 (p, J = 9.9, 8.7 Hz, 1H), 1.66 – 1.49 (m, 2H), 1.43 – 1.31 (m, 2H), 1.29 (s, 6H), 1.28 (s, 6H), 0.83 (td, J = 13.0, 5.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.72, 143.69, 137.68, 128.66, 128.13, 127.90, 127.78, 125.68, 125.13, 115.16, 82.78, 55.13, 48.35, 39.72, 39.16, 35.59, 32.69, 30.42, 25.29, 24.91, 22.08; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.98; IR (neat): 2956.9 (s), 2930.5 (s), 2872.6 (m), 1729.4 (s), 1457.5 (m), 1379.2 (m), 1288.9 (s), 1239.1 (w), 1141.6 (s), 1073.0 (m), 755.5 (m), 700.3 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{29}{}^{1}H_{40}{}^{11}B_{1}{}^{6}O_{2}$ $[M+H]^+$: calculated: 431.3121, found: 431.3115. The relative stereochemistry was assigned by X-ray crystallography.

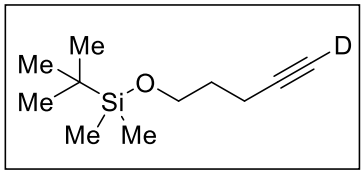




4,4,5,5-tetramethyl-2-((1*R*,2*R*)-1-phenethyl-2-((*R*)-1-phenylbut-3-en-1-yl)cyclopentyl)-1,3,2-dioxaborolane (38). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with (*E*)-2,2'-(1,8-diphenyloct-7- ene-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **(3.20)** (56.13 mg, 0.1 mmol), KO*t*-Bu (22.4 mg, 0.2 mmol) and toluene (0.5 mL). Upon

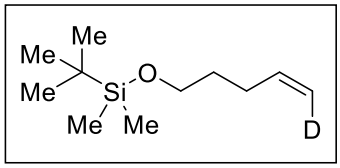
completion, the reaction mixture was quenched with allyl bromide (60.5 mg, 0.5 mmol), stir for another two hours, then diluted with diethyl ether (2 mL), filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (hexanes: ethyl acetate = 100 : 0.8, stain in CAM) to afford the desired product as a white solid (32.7 mg, 76%, >20:1 dr). ^{1}H and ^{13}C NMR spectral data and X-ray crystallographic data identical to that above.

3.7.9 ^{2}D-Labeled Experiment



***tert*-butyldimethyl((pent-4-yn-1-yl-5-*d*)oxy)silane (S3.14).** A flame dried 20 mL vial equipped with stir bar is charged with *tert*-butyldimethyl(pent-4-yn-1-yloxy)silane (1.87 g, 9.43 mmol, 1.0 equiv), then sealed and evacuated/backfilled with N_2 3x. Anhydrous THF (9.4 mL) is then charged in the vessel and the clear colorless solution set to stir at -78^{o}C. A solution of *n*BuLi in Hexanes (4.20 mL, 2.70 M, 11.3 mmol, 1.2 equiv) is then added dropwise, resulting in a clear, yellow solution. After stirring for 30min at -78^{o}C, the mixture is brought to 0^{o}C and allowed to stir an additional 20min. At this point, the reaction is quenched by slow addition of D_2O (853 μL, 47.2 mmol, 5.0 equiv), resulting in a white slurry. The resulting mixture is allowed to stir for 4h, then directly dried over Na_2SO_4 and passed through a pad of SiO_2, rinsing with Et_2O. Filtrate is then concentration to yield clear, colorless oil

(1.88 g, 9.43 mmol, quantitative). No further purification necessary. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.70 (t, *J* = 6.0 Hz, 2H), 2.27 (t, *J* = 7.1 Hz, 2H), 1.78 – 1.68 (m, 2H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 61.41, 31.51, 25.90, 18.29, 14.79, -5.39; IR (neat): 2988.3 (s), 2946.7 (w), 2870.2 (s), 1393.6 (w), 1142.5 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{11}{}^{1}H_{22}{}^{2}D_{1}{}^{29}Si_{1}{}^{16}O_{1}$ $[M+H]^{+}$: calculated: 200.1581, found: 200.1572.

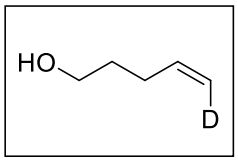


(*Z*)-*tert*-butyldimethyl((pent-4-en-1-yl-5-*d*)oxy)silane (S3.15). Adapted from published procedure.[85] A flame dried 250 mL round bottom equipped with magnetic stir bar is charged with **S3.14** (1.43 g, 7.2 mmol, 1.0 equiv) inside an argon-filled glovebox. *t*BuOH (990 mg, 13.4 mmol, 2.4 equiv) is then added to the vessel, followed by toluene (60 mL) then Polymethylhydrosiloxane (979 μL, 17.3 mmol (monomer), 2.4 equiv). The mixture is set to stir, then IPrCuO*t*Bu[86] (75.6 mg, 0.14 mmol, 2 mol%) is added, at which point bubbling is observed. The vessel is sealed with a rubber septum, then moved to the fume hood where it is allowed to stir for 1h at room temperature. At this point, the reaction mixture turns dark brown and it is passed through a pad of silica gel, rinsing with Et_2O. The filtrate is concentrated then SiO_2 chromatography performed (0%

[85]Lalic, G.; Whittaker, A. M. *Org. Lett.* **2013**, *15*, 1112-1115.

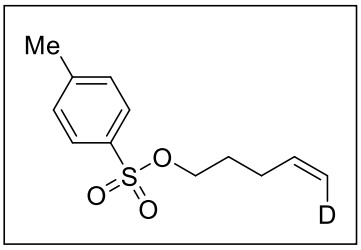
[86]For preparation see: Sadighi, J. P.; Mankad, N. P.; Laitar, D. S. *Organometallics*, **2004**, *23*, 3369-3371.

Et_2O/Pentanes, gradient to 2.5% Et_2O/Pentanes, visualizing with $KMnO_4$). Product coelutes with PMHS and yield is carried across two steps. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.85 – 5.77 (m, 1H), 4.94 (d, *J* = 10.2 Hz, 1H), 3.62 (t, *J* = 6.5 Hz, 2H), 2.10 (td, *J* = 7.6, 0.9 Hz, 2H), 1.64 – 1.58 (m, 2H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): 138.45 (s), 114.19 (t, *J*=23.5 Hz), 62.53 (s), 31.99 (s), 29.97 (s), 25.95 (s), 18.34 (s), -5.30 (s); IR (neat): 2987.3 (m), 2871.0 (m), 1142.4 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{11}{}^{1}H_{24}{}^{2}D_{1}{}^{29}Si_{1}{}^{16}O_{1}$ $[M+H]^+$: calculated: 202.1737, found: 202.1741.



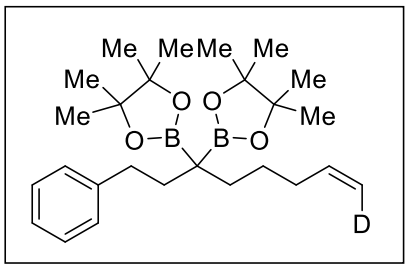
(*Z*)-pent-4-en-5-*d*-1-ol (S3.16). A 50 mL round bottom equipped with magnetic stir bar is charged with a solution of **S3.15** (1.36 g, 6.75 mmol, 1.0 equiv; mixed with PMHS, see above) in anhydrous THF (6.75 mL). The vessel and contents are then brought to 0°C, at which point TBAF solution in THF (16.8 mL, 1 M, 16.8 mmol, 2.5 equiv) is added dropwise (exothermic process). After addition, the mixture is allowed to stir at room temperature for 5h. The reaction mixture is then poured into a seperatory funnel containing ca. 10 mL brine and the organics are extracted 3x with ca. 10 mL Et_2O. Combined organics are then dried over Na_2SO_4 and concentrated to yield crude oil. Oil is purified by SiO_2 chromatography (2.5% Et_2O/Pentanes, gradient to 10% Et_2O/Pentanes, visualized with $KMnO_4$ to yield clear, colorless oil (343.9 mg, 3.95 mmol, 55% *across 2 steps*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.87 – 5.79 (m, 1H), 4.97 (d, *J* = 10.2 Hz, 1H), 3.67 (t, *J* = 6.5 Hz, 2H), 2.15 (td, *J* = 7.6, 0.8 Hz, 2H), 1.71 – 1.64 (m, 2H), 1.57 (br s, 1H); ^{13}C NMR (150 MHz,

$CDCl_3$): δ 138.15 (s), 114.65 (t, *J*=23.5 Hz), 62.50 (s), 31.80 (s), 30.04 (s); IR (neat): 2988.5 (w), 2869.8 (w), 1141.9 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_5{}^{1}H_{10}{}^{2}D_1{}^{16}O_1$ $[M+H]^+$: calculated: 88.0873, found: 88.0870.



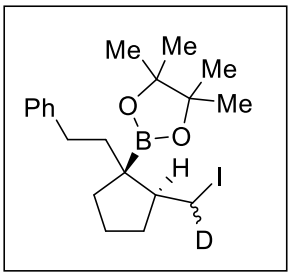
(*Z*)-pent-4-en-1-yl-5-*d*-4-methylbenzenesulfonate (S3.17). A flame dried 20 mL vial equipped with magnetic stir bar is charged with TsCl (904 mg, 4.74 mmol, 1.10 equiv) followed by DMAP (105 mg, 0.86 mmol, 0.20 equiv). The vial is sealed and evacuated/refilled with N_2 3x, then a solution of **S3.16** (375 mg, 4.31 mmol, 1.0 equiv) in anhydrous DCM (21.6 mL) is charged in. The mixture is brought to 0°C then reagent grade NEt_3 (720 μL, 5.17 mmol, 1.2 equiv) is added dropwise. The reaction is then allowed to stir at room temperature for 2h. At this point, the reaction mixture is treated with ca. 5 mL H_2O and the organics are extracted 3x with ca. 5 mL DCM. Combined organics are dried over Na_2SO_4 then concentrated to yield crude oil. Crude material is purified by SiO_2 chromatography (2.5% Et_2O/Pentanes, gradient to 10% Et_2O/Pentanes, visualized with CAM stain) to render clear, colorless oil (666 mg, 2.76 mmol, 64%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 5.72 – 5.64 (m, 1H), 4.94 (d, *J* = 10.1 Hz, 1H), 4.04 (t, *J* = 6.4 Hz, 2H), 2.45 (s, 3H), 2.08 (q, *J* = 7.1 Hz, 2H), 1.74 (p, *J* = 6.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 144.66 (s), 136.51 (s), 133.19 (s), 129.80 (s), 127.89 (s), 115.56 (t, *J*=23.6 Hz), 69.78 (s), 29.32 (s), 27.99 (s), 21.63 (s); IR (neat): 2957.1 (w), 1598.4 (w), 1359.0 (s),

1188.7 (s), 1097.8 (w), 928.0 (m), 810.6 (m), 664.2 (m), 554.6 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{12}{}^{1}H_{15}{}^{2}D_{1}{}^{32}S_{1}{}^{16}O_{3}{}^{23}Na_{1}$ $[M+Na]^{+}$: calculated: 264.0781, found: 264.0780.



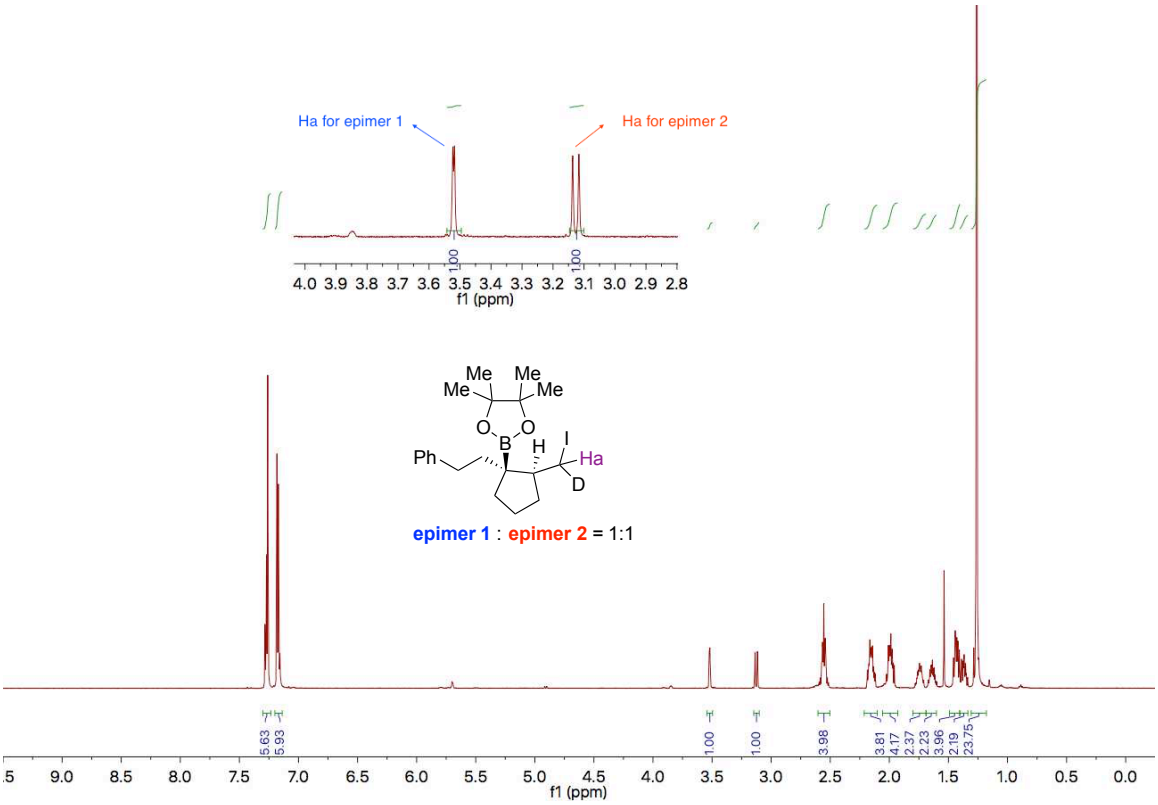
(*Z*)-2,2'-(1-phenyloct-7-ene-3,3-diyl-8-*d*)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.34). A flame dried 20 mL vial equipped with magnetic stir bar is charged with LTMP (405 mg, 2.75 mmol, 1.0 equiv) inside an argon-filled glovebox. The vial is sealed then moved to the hood where it is charged with anhydrous THF (9 mL). The orange solution is set to stir at 0°C then charged with a solution of **2.1** (1.02 g, 2.75 mmol, 1.0 equiv) in anhydrous THF (2 mL) where it is allowed to stir for 30 min. At this point, a solution of **S3.17** (663 mg, 2.75 mmol, 1.0 equiv) in anhydrous THF (2 mL) is added gradually. The mixture is brought to room temperature and allowed to stir overnight (23h). Upon return, the reaction mixture is diluted with Et_2O and passed through a pad of silica gel, rinsing with Et_2O. Filtrate is concentrated to render crude solid. Solid is purified by SiO_2 chromatography (0% EtOAc/Hexanes, gradient to 3% EtOAc/Hexanes, visualized with CAM stain). Product isolated as a white solid (938 mg, 2.13 mmol, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 – 7.21 (m, 2H), 7.22 – 7.16 (m, 2H), 7.16 – 7.10 (m, 1H), 5.89 – 5.80 (m, 1H), 4.92 (d, *J* = 10.3 Hz, 1H), 2.54 – 2.46 (m, 2H), 2.08 (q, *J* = 7.0 Hz, 2H), 1.93 – 1.86 (m, 2H), 1.75 – 1.69 (m, 2H), 1.42 – 1.34 (m, 2H), 1.23 (s, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 143.93 (s), 139.40 (s), 128.63 (s), 128.24 (s), 125.50 (s), 113.85 (t, *J*=23.5 Hz), 83.13 (s), 34.65

(s), 33.98 (s), 32.03 (s), 28.82 (s), 26.80 (s), 24.95 (s), 24.86 (s); IR (neat): 2978.5 (m), 2931.5 (w), 2858.9 (w), 1456.2 (w), 1378.6 (m), 1309.7 (s), 1255.2 (w), 1138.6 (s), 968.9 (w), 909.9 (m), 853.4 (m), 733.1 (s), 699.4 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{26}{}^{1}H_{42}{}^{2}D_{1}{}^{11}B_{2}{}^{16}O_{4}$ $[M+H]^{+}$: calculated: 442.3410, found: 442.3422.



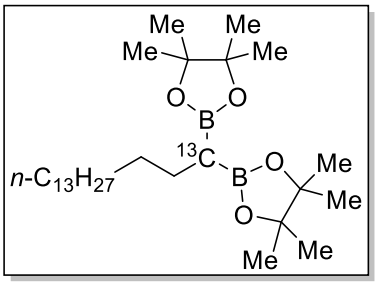
2-((1*R*,2*S*)-2-(iodomethyl-*d*)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.35). The reaction was performed according to *Representative Procedure for Deborylative Cyclization* with **3.34** (88.2 mg, 0.2 mmol, 1.00 equiv), KO*t*Bu (44.9 mg, 0.4 mmol, 2.0 equiv) in THF (1 mL) for 1h 30min. Yellow reaction mixture was then quenched with an I_2 solution in anhydrous THF (0.8 mL, 0.5 M, 0.4 mmol, 2.0 equiv), where the reaction turns white, then purple. The crude reaction mixture was purified by SiO_2 chromatography (0% EtOAc/Hexanes, gradient to 1% EtOAc/Hexanes, visualized with CAM stain) to afford a white solid (60.0 mg, 0.136 mmol, 68%; 1:1 mixture of epimers). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 – 7.25 (m, 2H), 7.20 – 7.15 (m, 3H), 3.52 (d, *J* = 3.1 Hz, 0.5H), 3.13 (d, *J* = 12.1 Hz, 0.5H), 2.60 – 2.51 (m, 2H), 2.20 – 2.11 (m, 2H), 2.03 – 1.94 (m, 2H), 1.79 – 1.70 (m, 1H), 1.68 – 1.59 (m, 1H), 1.47 – 1.40 (m, 2H), 1.40 – 1.33 (m, 1H), 1.26 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 143.11 (s), 128.37 (s), 128.22 (s), 125.64 (s), 83.30 (s), 53.87 (s), 53.84 (s), 41.19 (s), 41.17 (s), 36.11 (s), 36.08 (s), 33.91 (s), 33.88 (s), 25.12 (s), 24.82 (s), 21.86 (s), 21.84 (s), 11.49 (t, *J*=22.9 Hz), 11.47 (t, *J*=22.9 Hz) ; ^{11}B NMR (160 MHz, $CDCl_3$) δ

33.98; IR (neat): 2976.1 (m), 2930.8 (m), 2867.2 (w), 1454.0 (w), 1380.7 (s), 1311.3 (s), 1199.0 (w), 1141.5 (s), 966.9 (w), 853.6 (w), 748.3 (w), 698.5 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{20}{}^{1}H_{29}{}^{2}D_{1}{}^{11}B_{1}{}^{16}O_{2}{}^{127}I_{1}{}^{23}Na_{1}$ $[M+Na]^{+}$: calculated: 464.1344, found: 464.1339.

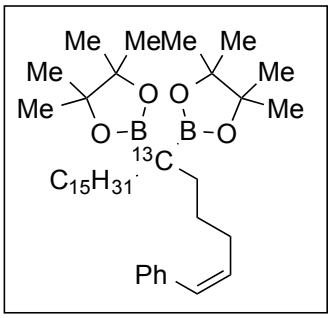


3.7.10 Analysis of Reaction Intermediates by ^{13}C-Labeled Experiments I

a) Preparation of ^{13}C-Labeled *geminal*-Diboronate Ester:



2,2'-(hexadecane-1,1-diyl-1-13C)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane (S3.18). Prepared from palmitic acid-1-^{13}C according to the literature procedure. The ^{1}H and ^{13}C NMR spectra were in accord with previously reported data.[87] ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.55-1.53 (m, 2H), 1.31-1.22 (m, 50H), 0.88 (t, J = 6.9 Hz, 3H), 0.71 (2dt, J = 111.5, 7.8 Hz, 1H).

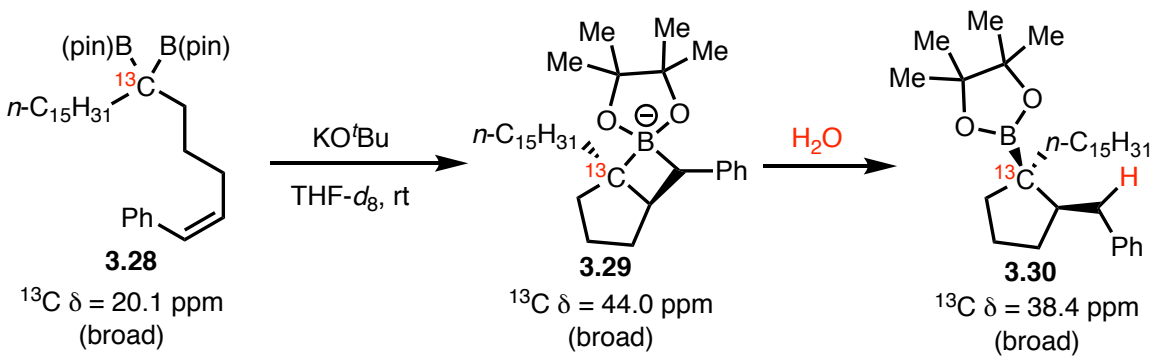


(*Z*)-2,2'-(1-phenylhenicos-1-ene-6,6-diyl-6-^{13}*C*)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.28). Prepared according to *Representative Procedure for Preparation of geminal-Diboronate Esters (Method C)* with **S3.18** (250 mg, 0.52 mmol), LTMP (92 mg, 0.624 mmol), (*Z*)-(5-bromopent-1-en-1-yl)benzene (141 mg, 0.624mmol) and THF (2.5 mL). The crude reaction mixture was purified by column chromatography on silica gel (100:1 hexanes/ethyl acetate, stain in CAM) to afford a colorless oil (191 mg, 59%). ^{1}H NMR

[87] K. Hong, X. Liu, and J. P. Morken *J. Am. Chem. Soc.* **2014**, *136,* 10581-10584.

(500 MHz, $CDCl_3$): δ 7.40 – 7.24 (m, 4H), 7.19 (t, *J* = 7.0 Hz, 1H), 6.36 (d, *J* = 11.7 Hz, 1H), 5.70 (dt, *J* = 11.8, 7.2 Hz, 1H), 2.60 – 2.22 (m, 2H), 1.71 – 1.63 (m, 2H), 1.59 (dt, *J* = 7.8, 4.1 Hz, 2H), 1.37 (t, *J* = 7.9 Hz, 2H), 1.31 – 1.22 (m, 26H), 1.21 (s, 24H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{1}H NMR (500 MHz, THF-d_8): δ 7.38 – 7.20 (m, 4H), 7.20 – 7.11 (m, 1H), 6.48 – 6.25 (d, *J* = 11.8 Hz, 1H), 5.71 – 5.58 (m, 1H), 2.36 – 2.22 (m, 2H), 1.67 – 1.52 (m, 4H), 1.48 – 1.37 (m, 2H), 1.29 (d, *J* = 2.6 Hz, 26H), 1.22 – 1.11 (m, 24H), 0.93 – 0.84 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.87, 133.55, 128.72, 128.34, 128.01, 126.26, 82.84, 31.91, 30.40, 30.36, 29.71, 29.69, 29.66, 29.65, 29.60, 29.34, 29.01, 28.94, 28.78, 28.70, 27.67, 27.12, 24.72, 22.67, 19.29, 14.09; ^{13}C NMR (125 MHz, THF-d_8): δ 139.00, 134.07, 129.71, 129.61, 128.94, 127.25, 83.55, 33.05, 31.73, 30.84, 30.78, 30.76, 30.48, 30.36, 28.81, 28.16, 23.73, 20.13(br, ***C***-B), 14.60; IR (neat): 2958.2 (m), 2924.6 (s), 2854.5 (m), 1729.3 (m), 1463.0 (w), 1377.4 (w), 1344.6 (w), 1288.6 (s), 1269.5 (s), 1138.7 (s), 1072.3 (w), 854.8 (w), 700.0 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{38}{}^{13}C_1{}^{1}H_{68}{}^{11}B_2{}^{16}O_4$ $[M+H]^+$: 624.5416, found: 624.5418.

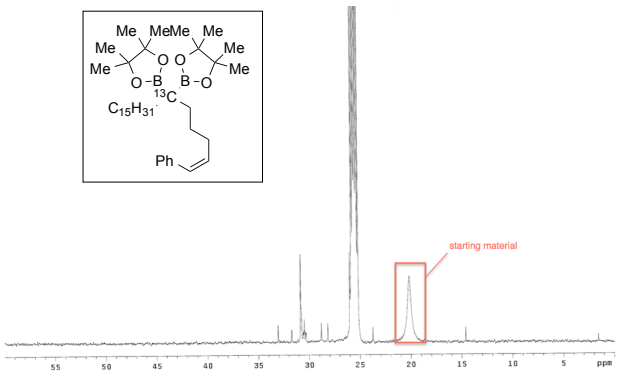
b) ^{13}C NMR Experiments



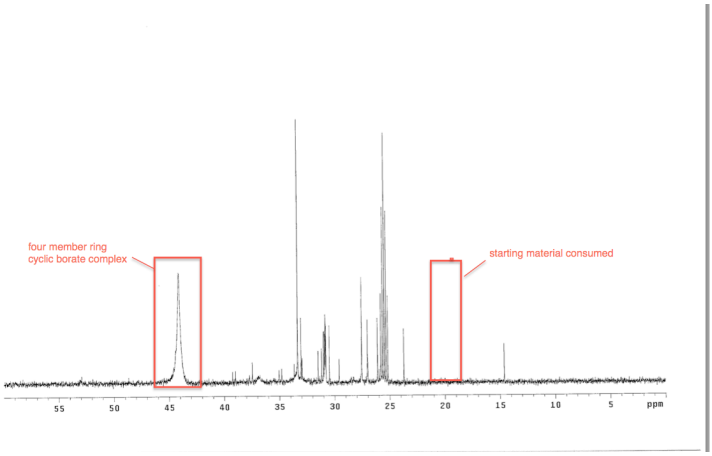
In the glove box, an oven-dried NMR tube is charged with diboronate ester **3.28** (31.2 mg, 0.05mmol), KO*t*-Bu (11.2 mg, 0.1 mmol) and THF-d_8 (0.60 mL). The NMR tube is then sealed with a rubber septum, removed from the glove box, and monitored by ^{13}C NMR at 25 ^{o}C. After 7 hours, water (2.7 mL, 0.15 mmol) is added via syringe, and the mixture again observed by ^{13}C NMR. At this point, the reaction mixture is diluted with diethyl ether, filtered through a silica gel plug, rinsed with diethyl ether, and concentrated *in vacuo*. The crude reaction mixture is purified on silica gel (hexanes: ethyl acetate = 100:0.6) to afford the desired product **3.30** (19.6 mg, 79% yield, d.r. > 10:1) together with protodeborylation byproduct (2.1 mg).

^{13}C NMR Spectra of the Reaction Mixture (125 MHz, THF-d_8, δ 10-60 ppm):

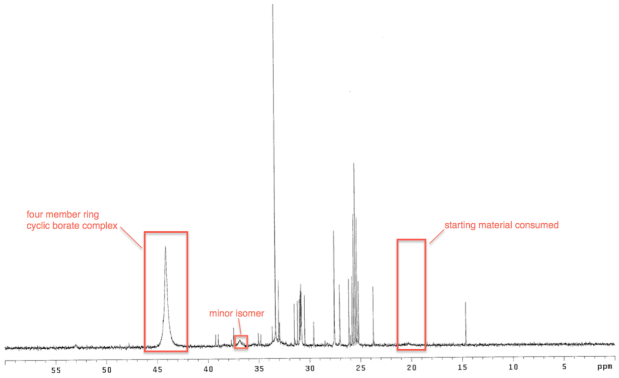
i. Diboronate ester **3.28**



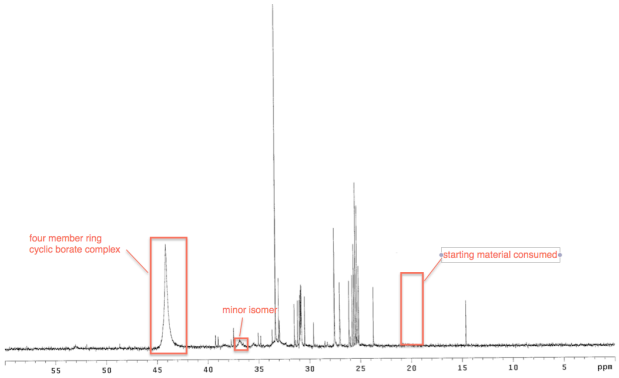
ii. **3.28** and KO*t*-Bu for 30 minutes



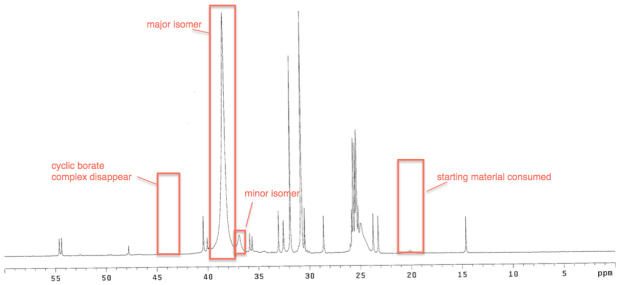
iii. **3.28** and KO*t*-Bu for 180 minutes



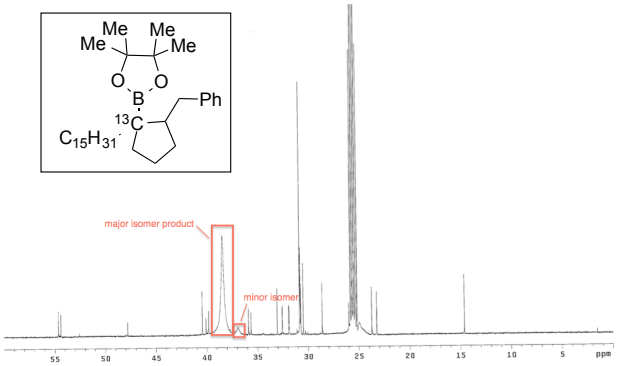
iv. **3.28** and KO*t*-Bu for 7 hours

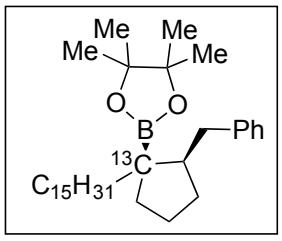


v. 1 minute after H_2O was added



vi. Isolated product, **3.30**

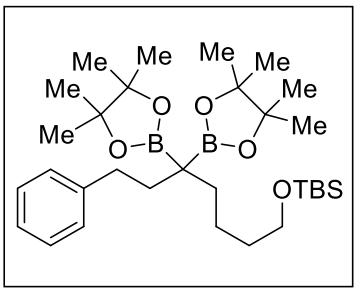




2-(2-benzyl-1-pentadecylcyclopentyl-1-^{13}C)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane. (**3.30, *major diastereomer***) ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 – 7.22 (m, 2H), 7.17 – 7.13 (m, 3H), 2.99 (dt, *J* = 13.4, 2.4 Hz, 1H), 2.32 (ddd, *J* = 13.1, 11.5, 1.4 Hz, 1H), 1.97 (dddd, *J* =

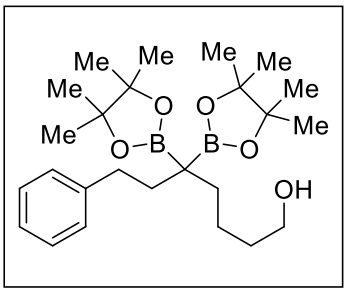
12.5, 8.7, 4.7, 1.5 Hz, 1H), 1.82 – 1.74 (m, 1H), 1.73 – 1.56 (m, 3H), 1.52 – 1.41 (m, 1H), 1.35 – 1.18 (m, 40H), 1.12 – 1.03 (m, 1H), 0.88 (t, J = 6.9 Hz, 3H); ^{1}H NMR (500 MHz, THF-d_8): δ 7.21 – 7.16 (m, 2H), 7.13 – 7.06 (m, 3H), 2.98 (dt, J = 13.5, 2.6 Hz, 1H), 2.41 – 2.28 (m, 1H), 2.08 – 1.96 (m, 1H), 1.90 – 1.78 (m, 1H), 1.67 – 1.52 (m, 2H), 1.51 – 1.41 (m, 2H), 1.37 – 1.23 (m, 38H), 1.22 – 1.14 (m, 2H), 1.11 – 1.02 (m, 1H), 0.89 (td, J = 6.9, 2.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.10, 128.82, 128.04, 125.36, 82.88, 53.07, 52.83, 46.76, 39.39, 38.80, 38.54, 37.36, 34.42, 34.17, 31.92, 31.33, 31.31, 30.72, 30.68, 29.72, 29.70, 29.65, 29.64, 29.36, 27.47, 25.16, 24.85, 24.81, 22.68, 22.40, 14.12; ^{13}C NMR (125 MHz, THF-d_8): δ 144.03, 144.00, 129.70, 129.64, 128.98, 128.95, 126.32, 83.89, 54.63, 54.40, 47.80, 40.44, 40.08, 39.81, 38.41, 35.89, 35.64, 33.06, 32.58, 32.55, 31.92, 31.88, 30.84, 30.80, 30.76, 30.74, 30.49, 28.63, 23.74, 23.25, 14.61; IR (neat): 2956.4 (m), 2923.6 (s), 2853.7 (m), 1728.8 (m), 1462.6 (w), 1378.0 (w), 1287.5 (m), 1141.5 (m), 1072.2 (w), 743.0 (w), 699.7 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{32}{}^{13}C_1{}^{1}H_{58}{}^{11}B_1{}^{16}O_2$ $[M+H]^+$: calculated: 498.4563, found: 498.4574.

3.7.11 Analysis of Reaction Intermediates by ^{13}C-Labeled Experiments II

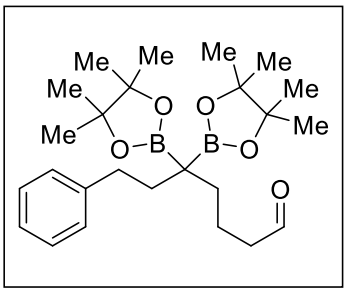


a) Preparation of ^{13}C-Labeled Alkene of *geminal*-Diboronate Ester *tert*-butyldimethyl((7-phenyl-5,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptyl)oxy)silane (S3.19).

The reaction was performed according to *Representative Procedure (Method C)* with diboronate ester **2.1** (372.3 mg, 1.0 mmol), LTMP (155 mg, 1.05 mmol), (4-bromobutoxy)(*tert*-butyl)dimethylsilane (294.0 mg, 1.10 mmol) and THF (4 mL). The crude reaction mixture was purified by column chromatography on silica gel (1% EtOAc/Hexanes, gradient to 3% EtOAc/Hexanes, visualized with CAM stain) to afford a clear, colorless oil (522.9 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 – 7.21 (m, 2H), 7.21 – 7.17 (m, 2H), 7.16 – 7.10 (m, 1H), 3.62 (t, J = 6.5 Hz, 2H), 2.55 – 2.45 (m, 2H), 1.94 – 1.84 (m, 2H), 1.76 – 1.66 (m, 2H), 1.58 – 1.49 (m, 2H), 1.38 – 1.27 (m, 2H), 1.23 (s, 24H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.83 (s), 128.50 (s), 128.07 (s), 125.32 (s), 82.95 (s), 63.52 (s), 33.88 (s), 33.84 (s), 31.91 (s), 29.01 (s), 26.00 (s), 24.81 (s), 24.70 (s), 23.63 (s), 18.34 (s), -5.22 (s); IR (neat): 2977.0 (w), 2928.8 (m), 2857.4 (w), 1349.2 (m), 1306.0 (m), 1253.9 (m), 1138.3 (s), 1101.4 (m), 850.4 (m), 835.8 (m), 775.0 (m), 699.0 (m) cm^{-1}. HRMS-(DART+) for $^{12}C_{31}{}^{1}H_{57}{}^{11}B_2{}^{16}O_5{}^{28}Si_1$ [M+H]: calculated: 559.4161, found: 559.4183.

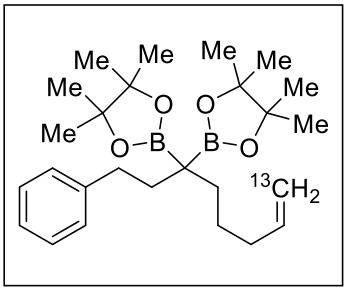


7-phenyl-5,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptan-1-ol (S3.20). A 20 mL vial containing **S3.19** (482 mg, 0.86 mmol, 1.0 equiv) and magnetic stirbar is loaded with reagent grade MeOH (6.9 mL, 0.125 M). The heterogeneous mixture is set to stir at room temperature, then *p*-TsOH monohydrate added (8.2 mg, 0.04 mmol, 0.05 equiv). The mixture almost immediately becomes homogeneous. Allowed to stir 1h at rt then volatile components removed *in vacuo*. Resulting crude oil is then purified by SiO_2 chromatography (5% EtOAc/Hexanes, gradient to 25% EtOAc/Hexanes, visualized with $KMnO_4$ stain). Product isolated as white solid (356.3 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 – 7.22 (m, 2H), 7.22 – 7.17 (m, 2H), 7.16 – 7.11 (m, 1H), 3.73 – 3.65 (m, 2H), 2.56 – 2.48 (m, 2H), 1.93 – 1.85 (m, 2H), 1.75 – 1.64 (m, 3H), 1.64 – 1.56 (m, 2H), 1.44 – 1.31 (m, 2H), 1.23 (s, 24H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.67 (s), 128.45 (s), 128.11 (s), 125.40 (s), 83.07 (s), 62.33 (s), 33.84 (s), 32.72 (s), 32.13 (s), 27.98 (s), 24.79 (s), 24.66 (s), 23.03 (s); IR (neat): 3457.7 (w, br), 2977.0 (w), 2929.0 (w), 2861.0 (w), 1348.8 (m), 1307.5 (s), 1250.7 (m), 1137.6 (s), 853.2 (m), 699.8 (w) cm^{-1}. HRMS-(DART+) for $^{12}C_{25}{}^{1}H_{43}{}^{11}B_2{}^{16}O_5$ [M+H]: calculated: 445.3297, found: 445.3286.



7-phenyl-5,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) heptanal (S31). A flame dried 20 mL vial equipped with magnetic stirbar is sealed with rubber septum then evacuated/backfilled with N_2 3x. The vial is then charged with $(COCl)_2$ (71.1 μL, 0.84 mmol, 1.4 equiv) followed by anhydrous DCM (0.3 mL). The solution is then set to stir at -78°C and anhydrous DMSO (119 μL, 1.67 mmol, 2.8 equiv) was added dropwise, significant gas evolution noted. The mixture was allowed to stir at -78°C for ca. 10min. A solution of **S3.20** in anhydrous DCM (0.3 mL) is then added dropwise, followed immediately by the slow addition of freshly distilled NEt_3 (507 μL, 3.64 mmol, 6.1 equiv; salt formation observed). The vessel and contents were then allowed to warm to room temperature and stir an additional 3h. Volatiles were then removed by high vacuum and the organics redissolved in EtOAc. Organics were washed with a saturated, aqueous Na_2CO_3 solution then concentrated to yield crude oil. Oil purified by SiO_2 chromatography (5% EtOAc/Hexanes, gradient to 10% EtOAc/Hexanes, visualized with CAM stain). Product isolated as white solid (232 mg, 0.52 mmol, 88%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.77 (s, 1H), 7.27 – 7.22 (m, 2H), 7.22 – 7.18 (m, 2H), 7.18 – 7.11 (m, 1H), 2.55 – 2.49 (m, 2H), 2.46 – 2.40 (m, 2H), 1.95 – 1.89 (m, 2H), 1.75 – 1.69 (m, 2H), 1.66 – 1.59 (m, 2H), 1.23 (s, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 203.07 (s), 143.53 (s), 128.48 (s), 128.14 (s), 125.45 (s), 83.12 (s), 44.61 (s), 33.83 (s), 31.89 (s), 28.98 (s), 24.81 (s), 24.72 (s), 19.86 (s); IR (neat): 2977.3 (w), 2931.7 (w),

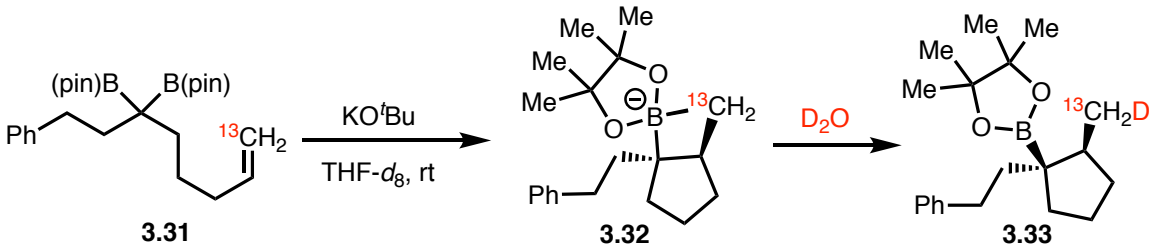
1708.3 (m), 1454.9 (w), 1310.4 (m), 1252.4 (m), 1137.5 (s), 853.9 (w) cm^{-1}. HRMS-(DART+) for $^{12}C_{25}{}^{1}H_{41}{}^{11}B_2{}^{16}O_5$ [M+H]: calculated: 443.3140, found: 443.3138.



2,2'-(1-phenyloct-7-ene-3,3-diyl-8-^{13}C)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.31). A flame dried, 20 mL vial equipped with magnetic stirbar is charged with Methyl-^{13}C-triphenylphosphonium iodide (212 mg, 0.52 mmol, 1 equiv) and KO*t*-Bu (59 mg, 0.52 mmol, 1 equiv) inside an argon-filled glovebox. Anhydrous THF is then charged into the vessel (1.5 mL) to give a vivid yellow solution. Vessel is sealed with a rubber septum and moved to the fume hood where it is allowed to stir for 1h at room temperature. A solution of **S31** (231 mg, 0.52 mmol, 1 equiv) in anhydrous THF (1.5 mL) is then added to the reaction vessel. The yellow color fades and a white suspension remains. The suspension is allowed to stir for 1.5h at room temperature at which point it is passed through a pad of SiO_2, rinsing with Et_2O. The resulting clear, colorless solution is concentrated to give a white solid. Product is isolated by SiO_2 chromatography (1% EtOAc/Hexanes, gradient to 5% EtOAc/Hexanes, visualized by CAM stain) to give white solid (208 mg, 0.47 mmol, 91%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26 – 7.22 (m, 2H), 7.22 – 7.18 (m, 2H), 7.16 – 7.09 (m, 1H), 5.86 (ddt, J = 16.8, 10.2, 6.6 Hz, 1H), 5.01 (ddd, J = 153.4, 17.2, 1.8 Hz, 1H), 4.93 (ddd, J = 156.8, 10.2, 2.0 Hz, 1H), 2.54 – 2.47 (m, 2H), 2.11 – 2.04 (m, 2H), 1.93 – 1.85 (m, 2H), 1.75 – 1.69 (m, 2H), 1.43 – 1.34 (m, 2H), 1.23 (s, 24H); ^{13}C NMR δ 143.78 (s), 139.33 (d, J =

69.2 Hz), 128.49 (s), 128.09 (s), 125.35 (s), 113.98 (s, ^{13}C), 82.98 (s), 34.55 (s), 33.83 (s), 31.88 (s), 28.66 (s), 26.65 (d, J = 3.6 Hz), 24.80 (s), 24.71 (s); IR (neat): 2977.9 (w), 2927.4 (w), 2858.9 (w), 1352.9 (w), 1307.7 (2), 1255.5 (w), 1139.2 (m), 855.6 (w) cm^{-1}. HRMS-(DART+) for $^{12}C_{25}{}^{13}C_1{}^{1}H_{43}{}^{11}B_2{}^{16}O_4$ [M+H]: calculated: 442.3381, found: 442.3388.

b) ^{13}C NMR Experiments of ^{13}C-Labeled *geminal*-Diboronate Ester



3.31

^{13}C δ = 114.5 ppm
(sharp)

3.32

^{13}C δ = 26.9 ppm
(broad)

3.33

^{13}C δ = 20.6 ppm
(triplet)

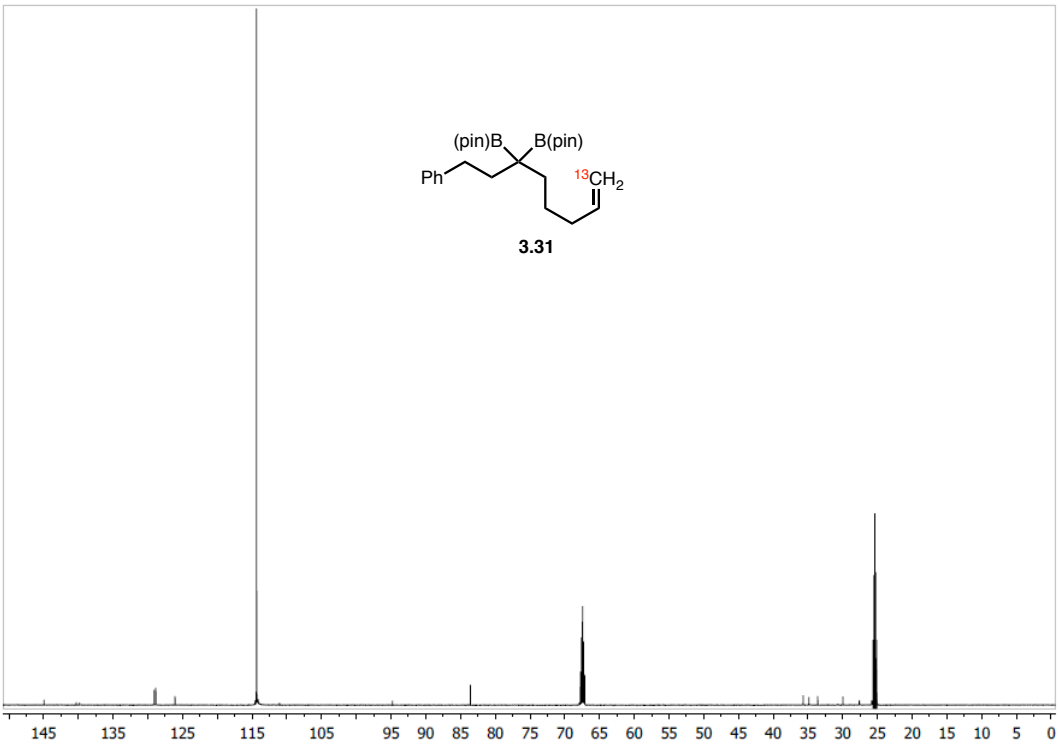


Figure S3.5 - ^{13}C labeled starting material (3.31) in d_8-THF

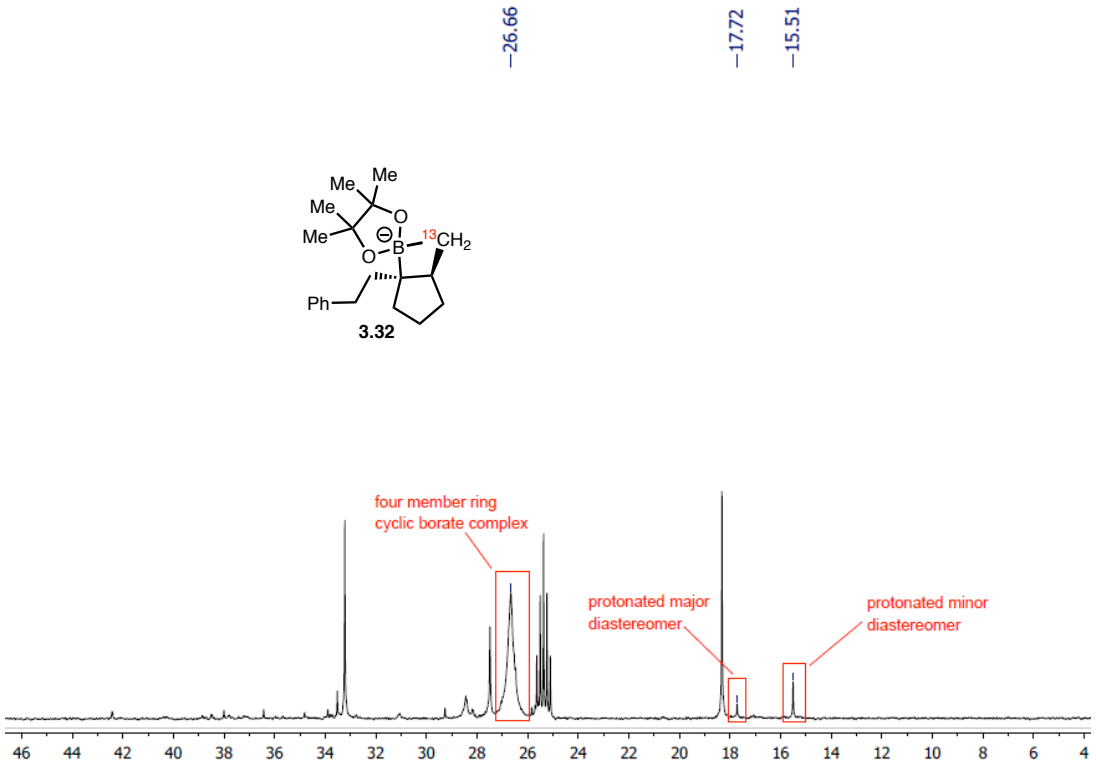


Figure 3.6 – 3.31 with KOt-Bu for 20 minutes in d_8-THF (zoomed in on significant region for clarity)

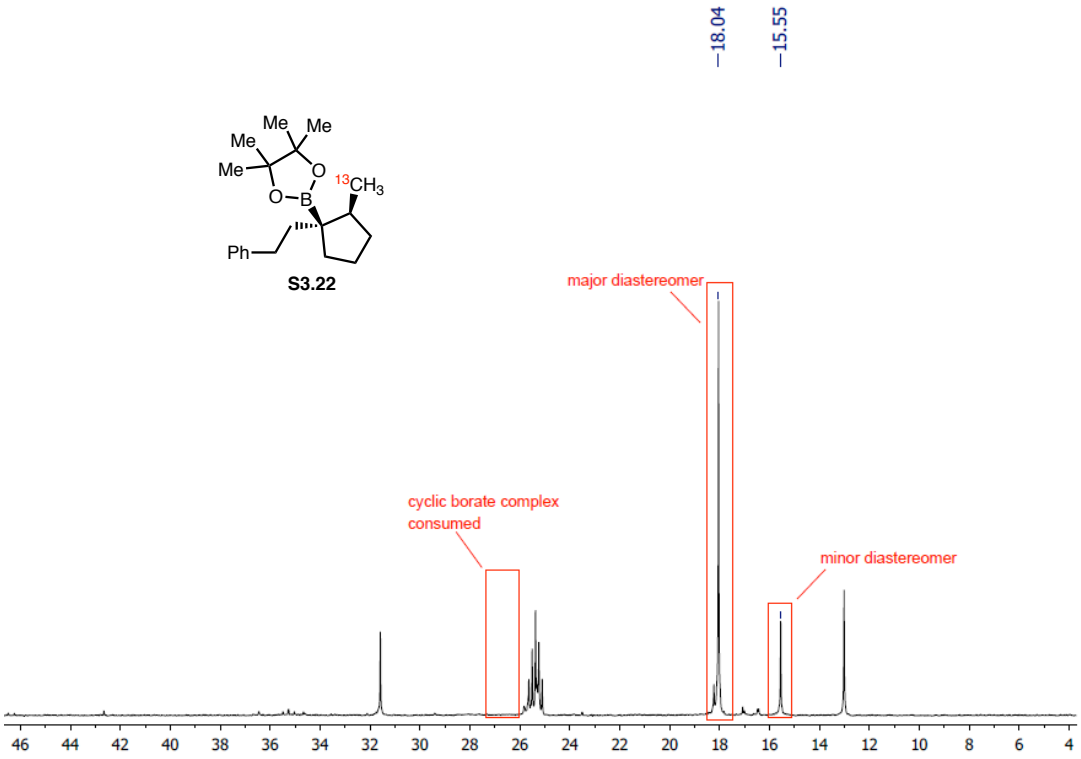


Figure 7.3 – 1 minute after addition of H_2O

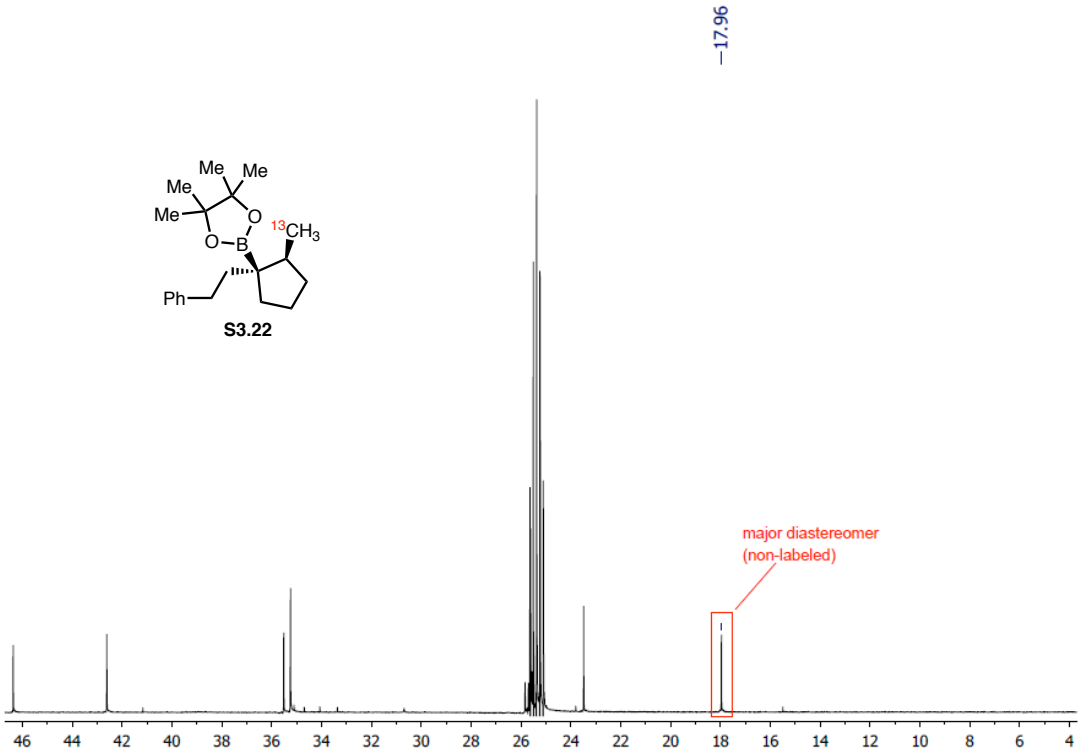


Figure 3.4 - Isolated major product (non-^{13}C labeled) in d_8-THF

3.7.12 X-ray crystallographic data

X-ray crystallographic data for **2-((1*R*,2*S*)-2-(iodomethyl)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Compound 3.9).**

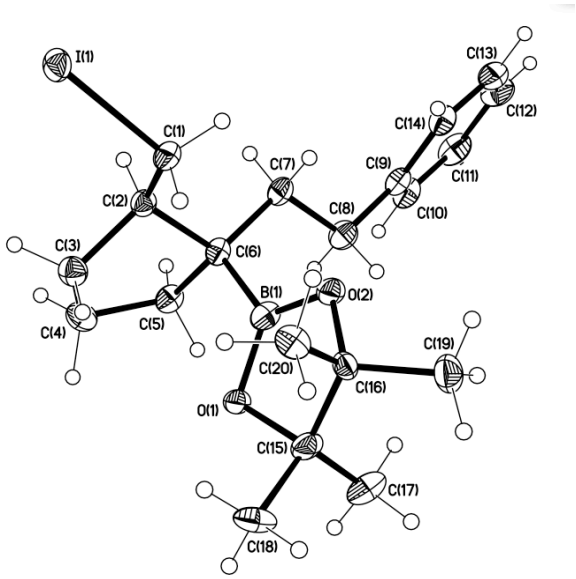


Table S3.2.

Crystal data and structure refinement for **2-((1*R*,2*S*)-2-(iodomethyl)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane**. **(Compound 3.9).**

Identification code	$C_{20}H_{30}BIO_2$	
Empirical formula	$C_{20}H_{30}BIO_2$	
Formula weight	440.15	
Temperature	100(2) K	
Wavelength	0.71073 ≈	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 6.5129(8) ≈	a= 99.987(2)∞.
	b = 13.4237(16) ≈	b= 95.992(2)∞.
	c = 23.452(3) ≈	g = 96.163(2)∞.
Volume	1991.7(4) $\approx^3$	
Z	4	
Density (calculated)	1.468 Mg/m^3	
Absorption coefficient	1.617 mm^{-1}	
F(000)	896	

Crystal size	0.400 x 0.210 x 0.150 mm^3
Theta range for data collection	1.639 to 28.450∞.
Index ranges	-8<=h<=8, -17<=k<=17, -31<=l<=31
Reflections collected	38081
Independent reflections	10019 [R(int) = 0.0443]
Completeness to theta = 25.242∞	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7457 and 0.6368
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10019 / 1 / 500
Goodness-of-fit on F^2	1.014
Final R indices [I>2sigma(I)]	R1 = 0.0315, wR2 = 0.0648
R indices (all data)	R1 = 0.0501, wR2 = 0.0718
Extinction coefficient	na
Largest diff. peak and hole	1.372 and -0.705 e.≈$^{-3}$

Table S3.3.

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (≈^{2}x 10^3)

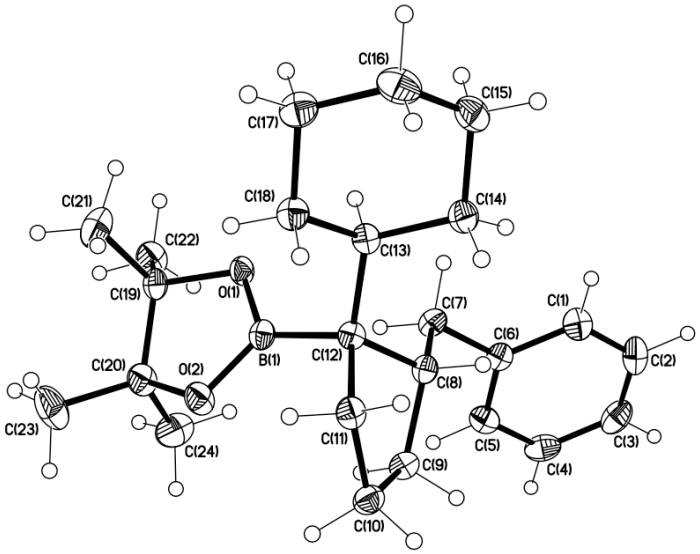
for C20H30BIO2. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
I(1)	-2688(1)	8964(1)	2686(1)	22(1)
O(2)	53(3)	6298(1)	3911(1)	20(1)
B(1)	1532(5)	7128(2)	4056(1)	21(1)

C(1)	-1455(4)	8104(2)	3314(1)	20(1)
C(2)	292(4)	8747(2)	3743(1)	18(1)
C(3)	2305(4)	8995(2)	3486(1)	22(1)
C(4)	3922(4)	9401(2)	4024(1)	24(1)
C(5)	3035(4)	8990(2)	4538(1)	20(1)
C(6)	1022(4)	8255(2)	4272(1)	17(1)
C(7)	-613(4)	8255(2)	4702(1)	20(1)
C(8)	141(4)	7877(2)	5255(1)	24(1)
C(9)	-1343(4)	7918(2)	5712(1)	20(1)
C(10)	-665(4)	8360(2)	6286(1)	26(1)
C(11)	-1990(5)	8377(2)	6714(1)	30(1)
C(12)	-4042(5)	7939(2)	6566(1)	31(1)
C(13)	-4752(4)	7494(2)	5993(1)	28(1)
C(14)	-3424(4)	7487(2)	5567(1)	22(1)
O(1)	3490(10)	6911(6)	3899(3)	18(1)
C(15)	3369(4)	5794(2)	3800(1)	24(1)
C(16)	971(8)	5454(4)	3569(3)	17(1)
C(17)	4185(11)	5443(5)	4300(3)	28(2)
C(18)	4715(9)	5507(5)	3275(3)	26(1)
C(19)	138(11)	4472(5)	3748(3)	29(2)
C(20)	314(7)	5426(4)	2926(2)	22(1)
O(1X)	3508(11)	6877(7)	4129(3)	18(1)
C(15X)	3369(4)	5794(2)	3800(1)	24(1)
C(16X)	1111(8)	5382(4)	3915(3)	21(1)
C(17X)	5083(10)	5330(6)	4167(4)	27(2)
C(18X)	3761(13)	5791(6)	3223(3)	33(2)
C(19X)	925(10)	5039(5)	4499(3)	31(2)
C(20X)	69(12)	4557(6)	3430(4)	37(2)
I(2)	1188(1)	-112(1)	1601(1)	24(1)
O(3)	7717(3)	2663(1)	800(1)	22(1)
O(4)	4297(3)	2481(1)	432(1)	21(1)
B(2)	5722(4)	2670(2)	924(1)	15(1)
C(21)	2576(4)	1186(2)	1285(1)	20(1)
C(22)	4214(4)	1849(2)	1738(1)	17(1)

C(23)	6177(4)	1364(2)	1884(1)	24(1)
C(24)	7890(4)	2260(2)	2137(1)	27(1)
C(25)	6965(4)	3230(2)	2028(1)	22(1)
C(26)	5057(4)	2869(2)	1558(1)	16(1)
C(27)	3411(4)	3617(2)	1599(1)	18(1)
C(28)	4219(4)	4659(2)	1471(1)	21(1)
C(29)	2722(4)	5441(2)	1529(1)	18(1)
C(30)	3393(4)	6433(2)	1827(1)	21(1)
C(31)	2049(4)	7166(2)	1876(1)	25(1)
C(32)	-7(4)	6927(2)	1629(1)	26(1)
C(33)	-689(4)	5951(2)	1328(1)	26(1)
C(34)	644(4)	5209(2)	1282(1)	23(1)
C(35)	7617(4)	2262(2)	171(1)	24(1)
C(36)	5453(4)	2521(2)	-69(1)	19(1)
C(37)	7693(5)	1120(2)	109(1)	40(1)
C(38)	9428(4)	2782(3)	-62(1)	43(1)
C(39)	5514(5)	3600(2)	-188(1)	33(1)
C(40)	4339(4)	1753(2)	-595(1)	30(1)

X-ray crystallographic data for compound **2-((1*R*,2*R*)-2-benzyl-1-cyclohexylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolan**



e (Compound 3.16).

Table S3.4.

Crystal data and structure refinement for **2-((1*R*,2*R*)-2-benzyl-1-cyclohexylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolan e (Compound 3.16).**

Identification code	$C_{24}H_{37}BO_2$	
Empirical formula	$C_{24}H_{37}BO_2$	
Formula weight	368.34	
Temperature	100(2) K	
Wavelength	0.71073 ≈	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 9.6816(10) ≈	a= 90∞.
	b = 18.2436(19) ≈	b= 106.083(2)∞.
	c = 12.6856(13) ≈	g = 90∞.
Volume	2152.9(4) $≈^3$	
Z	4	

Density (calculated)	1.136 Mg/m^3
Absorption coefficient	0.069 mm^{-1}
F(000)	808
Crystal size	0.400 x 0.250 x 0.180 mm^3
Theta range for data collection	1.671 to 28.339∞.
Index ranges	-12<=h<=12, -24<=k<=24, -16<=l<=16
Reflections collected	38756
Independent reflections	10716 [R(int) = 0.0408]
Completeness to theta = 25.242∞	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7457 and 0.6888
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10716 / 1 / 496
Goodness-of-fit on F^2	1.057
Final R indices [I>2sigma(I)]	R1 = 0.0443, wR2 = 0.0949
R indices (all data)	R1 = 0.0609, wR2 = 0.1035
Extinction coefficient	na
Largest diff. peak and hole	0.249 and -0.204 $e.\approx^{-3}$

Table S3.5.

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (≈^{2}x 10^3)

for c24h37bo2. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	6063(2)	4076(1)	7419(1)	19(1)
O(2)	6763(2)	5252(1)	7239(1)	24(1)
B(1)	6938(3)	4526(2)	7027(2)	18(1)
C(1)	11365(3)	2530(1)	8609(2)	25(1)
C(2)	12672(3)	2314(2)	9307(2)	29(1)
C(3)	13283(3)	2698(2)	10260(2)	29(1)
C(4)	12581(3)	3300(2)	10513(2)	28(1)
C(5)	11273(3)	3523(1)	9810(2)	23(1)
C(6)	10647(2)	3139(1)	8850(2)	19(1)
C(7)	9233(2)	3383(1)	8077(2)	21(1)
C(8)	9426(2)	3951(1)	7244(2)	18(1)
C(9)	10151(2)	4665(1)	7754(2)	20(1)
C(10)	9808(2)	5230(1)	6811(2)	23(1)
C(11)	8642(2)	4870(1)	5868(2)	20(1)
C(12)	8029(2)	4227(1)	6396(2)	17(1)
C(13)	7216(2)	3644(1)	5562(2)	18(1)
C(14)	8149(3)	3167(1)	5037(2)	23(1)
C(15)	7238(3)	2616(1)	4224(2)	27(1)
C(16)	6051(3)	2994(2)	3343(2)	31(1)
C(17)	5109(3)	3456(1)	3861(2)	26(1)
C(18)	6018(2)	4008(1)	4658(2)	21(1)
C(19)	5048(2)	4539(1)	7778(2)	21(1)

C(20)	5866(3)	5281(1)	7999(2)	24(1)
C(21)	3694(3)	4582(2)	6819(2)	33(1)
C(22)	4731(3)	4186(1)	8765(2)	28(1)
C(23)	4945(3)	5960(2)	7749(2)	38(1)
C(24)	6899(3)	5330(2)	9148(2)	35(1)
O(3)	1073(2)	6054(1)	2477(1)	20(1)
O(4)	1855(2)	4917(1)	2164(1)	23(1)
B(2)	1950(3)	5655(1)	2006(2)	18(1)
C(25)	6537(3)	7496(1)	3698(2)	26(1)
C(26)	7861(3)	7636(2)	4440(2)	33(1)
C(27)	8243(3)	7291(2)	5448(2)	32(1)
C(28)	7300(3)	6804(1)	5718(2)	29(1)
C(29)	5981(3)	6663(1)	4973(2)	24(1)
C(30)	5581(2)	7007(1)	3951(2)	20(1)
C(31)	4174(2)	6830(1)	3121(2)	20(1)
C(32)	4379(2)	6281(1)	2263(2)	18(1)
C(33)	5108(2)	5562(1)	2723(2)	22(1)
C(34)	4916(3)	5073(1)	1708(2)	24(1)
C(35)	3644(2)	5405(1)	814(2)	20(1)
C(36)	2997(2)	6011(1)	1393(2)	16(1)
C(37)	2178(2)	6619(1)	607(2)	17(1)
C(38)	3124(3)	7113(1)	117(2)	22(1)
C(39)	2237(3)	7686(1)	-658(2)	28(1)
C(40)	1044(3)	7337(2)	-1563(2)	32(1)
C(41)	82(3)	6861(2)	-1076(2)	28(1)
C(42)	968(3)	6282(1)	-312(2)	22(1)
C(43)	556(2)	5554(1)	3189(2)	22(1)
C(44)	711(3)	4793(1)	2691(2)	23(1)
C(45)	-962(3)	5768(2)	3167(2)	31(1)
C(46)	1562(3)	5657(2)	4346(2)	33(1)
C(47)	-614(3)	4567(2)	1789(2)	36(1)
C(48)	1180(3)	4174(2)	3511(2)	35(1)

X-ray crystallographic data for compound **2-((1*R*,2*R*)-2-benzyl-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Compound 3.21, major diastereomer).**

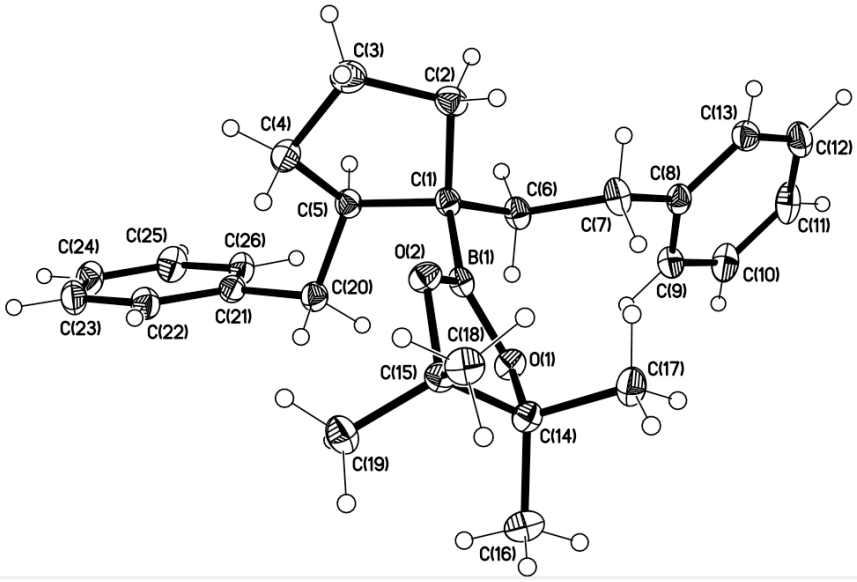


Table S3.6.

Crystal data and structure refinement for **2-((1*R*,2*R*)-2-benzyl-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Compound 3.21, major diastereomer).**

Identification code	$C_{26}H_{35}BO_2$
Empirical formula	$C_{26}H_{35}BO_2$
Formula weight	390.35
Temperature	100(2) K
Wavelength	0.71073 ≈
Crystal system	Monoclinic
Space group	$P2_1/n$
Unit cell dimensions	a = 11.0652(19) ≈ a= 90∞.

	b = 17.228(3) ≈	b= 98.660(3)∞.
	c = 11.842(2) ≈	g = 90∞.
Volume	2231.7(7) ≈^{3}	
Z	4	
Density (calculated)	1.162 Mg/m^3	
Absorption coefficient	0.070 mm^{-1}	
F(000)	848	
Crystal size	0.530 x 0.400 x 0.220 mm^3	
Theta range for data collection	2.103 to 28.324∞.	
Index ranges	-14<=h<=14, -22<=k<=20, -15<=l<=15	
Reflections collected	43822	
Independent reflections	5557 [R(int) = 0.0352]	
Completeness to theta = 25.242∞	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.7070	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5557 / 0 / 266	
Goodness-of-fit on F^2	1.048	
Final R indices [I>2sigma(I)]	R1 = 0.0386, wR2 = 0.0983	
R indices (all data)	R1 = 0.0474, wR2 = 0.1046	
Extinction coefficient	na	
Largest diff. peak and hole	0.390 and -0.188 e.≈$^{-3}$	

Table S3.7.

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (≈^{2}x 10^3)

for C26H35BO2. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
B(1)	3744(1)	6957(1)	6459(1)	16(1)
C(1)	4240(1)	6174(1)	6004(1)	16(1)
C(2)	3572(1)	5462(1)	6436(1)	20(1)
C(3)	4263(1)	5252(1)	7628(1)	25(1)
C(4)	5459(1)	5724(1)	7780(1)	21(1)
C(5)	5581(1)	6018(1)	6580(1)	17(1)
C(6)	4146(1)	6187(1)	4692(1)	19(1)
C(7)	2834(1)	6200(1)	4049(1)	22(1)
C(8)	2736(1)	6139(1)	2762(1)	19(1)
C(9)	3493(1)	6557(1)	2143(1)	24(1)
C(10)	3359(1)	6505(1)	960(1)	28(1)
C(11)	2472(1)	6028(1)	371(1)	28(1)
C(12)	1717(1)	5606(1)	971(1)	26(1)
C(13)	1848(1)	5658(1)	2154(1)	21(1)
C(14)	2901(1)	8165(1)	6432(1)	17(1)
C(15)	3167(1)	7859(1)	7684(1)	17(1)
C(16)	3325(1)	8988(1)	6262(1)	25(1)
C(17)	1568(1)	8068(1)	5898(1)	23(1)
C(18)	2107(1)	7938(1)	8356(1)	22(1)
C(19)	4338(1)	8192(1)	8354(1)	24(1)
C(20)	6468(1)	6702(1)	6570(1)	19(1)
C(21)	7791(1)	6466(1)	6917(1)	18(1)

C(22)	8387(1)	6573(1)	8030(1)	22(1)
C(23)	9608(1)	6368(1)	8336(1)	25(1)
C(24)	10256(1)	6054(1)	7529(1)	26(1)
C(25)	9672(1)	5936(1)	6420(1)	26(1)
C(26)	8448(1)	6137(1)	6121(1)	22(1)
O(1)	3615(1)	7630(1)	5831(1)	18(1)
O(2)	3387(1)	7033(1)	7515(1)	18(1)

X-ray crystallographic data for **4,4,5,5-tetramethyl-2-((1*R*,2*R*)-1-phenethyl-2-((*R*)-1-phenylbut-3-en-1-yl)cyclopentyl)-1,3,2-dioxaborolane (Compound 3.56).**

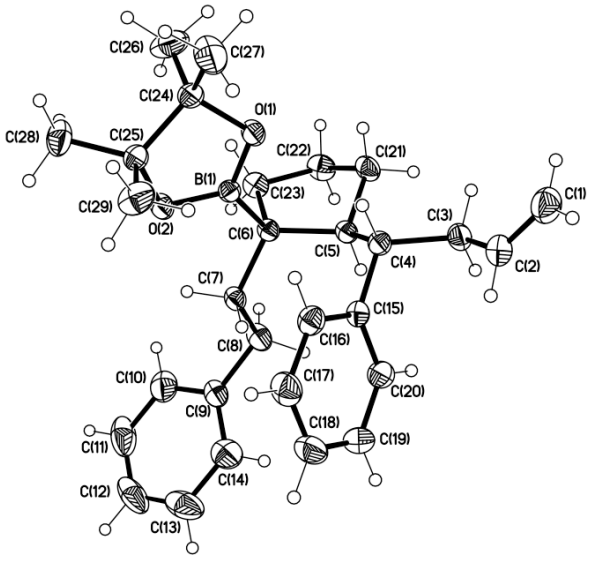


Table S3.8.

Crystal data and structure refinement for **4,4,5,5-tetramethyl-2-((1*R*,2*R*)-1-phenethyl-2-((*R*)-1-phenylbut-3-en-1-yl)cyclopentyl)-1,3,2-dioxaborolane (Compound 3.56).**

Identification code	C29H39BO2	
Empirical formula	C29 H39BO2	
Formula weight	430.41	
Temperature	173(2) K	
Wavelength	1.54178 ≈	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.9886(5) ≈	a= 69.073(2)∞.
	b = 10.2525(5) ≈	b= 84.917(2)∞.
	c = 13.6756(7) ≈	g = 76.535(2)∞.
Volume	1272.13(11) ≈^{3}	
Z	2	
Density (calculated)	1.124 Mg/m^3	
Absorption coefficient	0.516 mm^{-1}	
F(000)	468	
Crystal size	0.520 x 0.400 x 0.080 mm^3	
Theta range for data collection	3.460 to 66.686∞.	
Index ranges	-11<=h<=11, -12<=k<=12, -16<=l<=16	
Reflections collected	24493	
Independent reflections	4448 [R(int) = 0.0249]	
Completeness to theta = 66.750∞	98.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7528 and 0.6785	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4448 / 0 / 293	
Goodness-of-fit on F^2	1.027	
Final R indices [I>2sigma(I)]	R1 = 0.0393, wR2 = 0.0981	
R indices (all data)	R1 = 0.0407, wR2 = 0.0993	
Extinction coefficient	na	

Largest diff. peak and hole 0.313 and -0.208 e.≈$^{-3}$

Table S3.9.

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (≈^{2}x 10^3) for $C_{29}H_{39}BO_2$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	1652(1)	3532(1)	4221(1)	33(1)
O(2)	3289(1)	1550(1)	4287(1)	28(1)
B(1)	2635(1)	2887(1)	3680(1)	22(1)
C(1)	2312(2)	9366(2)	2921(1)	47(1)
C(2)	3111(1)	8405(1)	2586(1)	38(1)
C(3)	2640(1)	7591(1)	2017(1)	31(1)
C(4)	3085(1)	5954(1)	2560(1)	25(1)
C(5)	2623(1)	5150(1)	1936(1)	24(1)
C(6)	2891(1)	3481(1)	2455(1)	23(1)
C(7)	4324(1)	2676(1)	2218(1)	25(1)
C(8)	4718(1)	2968(1)	1061(1)	36(1)
C(9)	6021(1)	1925(1)	966(1)	34(1)
C(10)	5970(2)	619(2)	909(1)	47(1)
C(11)	7174(2)	-372(2)	882(1)	66(1)
C(12)	8432(2)	-70(2)	912(1)	70(1)
C(13)	8499(2)	1219(2)	968(1)	62(1)
C(14)	7301(2)	2214(2)	996(1)	45(1)
C(15)	4629(1)	5496(1)	2730(1)	26(1)
C(16)	5180(1)	4679(1)	3714(1)	32(1)
C(17)	6591(1)	4191(2)	3858(1)	42(1)
C(18)	7480(1)	4540(2)	3019(1)	44(1)
C(19)	6948(1)	5389(2)	2037(1)	41(1)

C(20)	5542(1)	5858(1)	1894(1)	33(1)
C(21)	1088(1)	5601(1)	1657(1)	31(1)
C(22)	902(1)	4471(1)	1239(1)	35(1)
C(23)	1712(1)	3076(1)	1998(1)	30(1)
C(24)	1417(1)	2419(1)	5208(1)	32(1)
C(25)	2800(1)	1298(1)	5365(1)	27(1)
C(26)	222(1)	1858(2)	5013(1)	58(1)
C(27)	1065(2)	3067(2)	6056(1)	59(1)
C(28)	2684(2)	-255(1)	5849(1)	43(1)
C(29)	3884(1)	1544(2)	5945(1)	43(1)

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X-ray crystallographic data for compound **2-((1*R*,2*R*)-2-((*R*)-1,2-diphenylethyl)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Compound 3.15).**

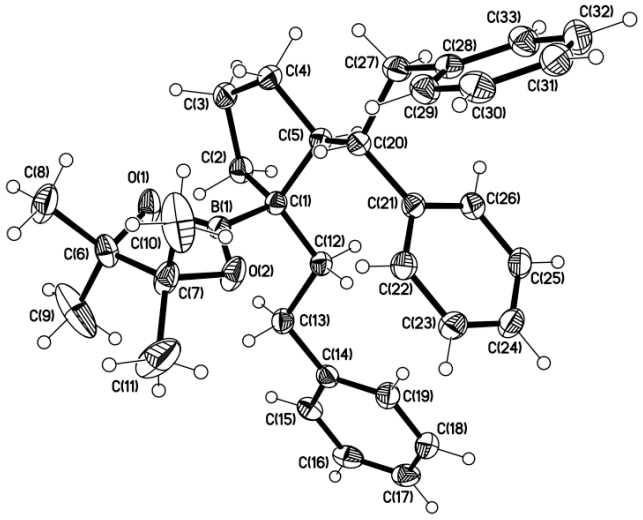


Table S3.10.

Crystal data and structure refinement for **2-((1*R*,2*R*)-2-((*R*)-1,2-diphenylethyl)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Compound 3.15).**

Identification code	$C_{33}H_{41}BO_2$	
Empirical formula	$C_{33}H_{41}BO_2$	
Formula weight	480.47	
Temperature	100(2) K	
Wavelength	0.71073 ≈	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 13.8342(16) ≈	a= 90∞.
	b = 17.292(2) ≈	b= 90∞.
	c = 23.666(3) ≈	g = 90∞.
Volume	5661.4(11) $≈^3$	
Z	8	
Density (calculated)	1.127 Mg/m^3	
Absorption coefficient	0.067 mm^{-1}	
F(000)	2080	
Crystal size	0.550 x 0.380 x 0.180 mm^3	
Theta range for data collection	1.721 to 28.335∞.	
Index ranges	-18<=h<=18, -23<=k<=22, -31<=l<=31	
Reflections collected	94700	
Independent reflections	7044 [R(int) = 0.0525]	
Completeness to theta = 25.242∞	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.7017	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7044 / 821 / 406	
Goodness-of-fit on F^2	1.028	

Final R indices [I>2sigma(I)]	R1 = 0.0439, wR2 = 0.1041
R indices (all data)	R1 = 0.0649, wR2 = 0.1172
Extinction coefficient	na
Largest diff. peak and hole	0.320 and -0.237 e.≈$^{-3}$

Table S3.11.

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (≈^{2}x 10^3)

for C33H41BO2. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	5645(1)	1765(1)	4124(1)	33(1)
O(2)	5909(1)	2977(1)	4455(1)	33(1)
C(6)	5676(1)	1686(1)	4741(1)	27(1)
C(7)	5546(1)	2534(1)	4940(1)	31(1)
C(8)	4873(2)	1142(1)	4932(1)	42(1)
C(9)	6661(2)	1356(2)	4881(1)	72(1)
C(10)	4480(2)	2753(1)	5008(1)	57(1)
C(11)	6116(3)	2768(2)	5452(1)	75(1)
O(1X)	5206(10)	1976(8)	4159(4)	36(3)
O(2X)	6309(10)	2822(9)	4479(5)	32(3)
C(6X)	5140(10)	1968(9)	4782(5)	43(3)
C(7X)	6040(10)	2389(9)	4986(5)	37(3)
C(8X)	4178(15)	2328(17)	4931(12)	84(7)
C(9X)	5248(19)	1109(11)	4917(13)	53(6)
C(10X)	5920(30)	2950(18)	5468(12)	49(5)
C(11X)	6951(15)	1978(16)	5134(11)	82(6)
B(1)	5869(1)	2514(1)	3994(1)	21(1)
C(1)	6077(1)	2810(1)	3372(1)	20(1)
C(2)	6219(1)	2117(1)	2963(1)	25(1)
C(3)	5199(1)	1834(1)	2804(1)	29(1)
C(4)	4509(1)	2497(1)	2966(1)	26(1)
C(5)	5157(1)	3196(1)	3107(1)	21(1)

C(12)	6954(1)	3358(1)	3365(1)	21(1)
C(13)	7903(1)	2997(1)	3563(1)	24(1)
C(14)	8758(1)	3546(1)	3539(1)	22(1)
C(15)	9683(1)	3258(1)	3433(1)	26(1)
C(16)	10479(1)	3747(1)	3407(1)	31(1)
C(17)	10366(1)	4538(1)	3484(1)	32(1)
C(18)	9455(1)	4833(1)	3593(1)	31(1)
C(19)	8658(1)	4343(1)	3621(1)	28(1)
C(20)	4625(1)	3832(1)	3443(1)	22(1)
C(21)	5249(1)	4538(1)	3565(1)	22(1)
C(22)	5498(1)	4731(1)	4119(1)	25(1)
C(23)	6105(1)	5355(1)	4232(1)	30(1)
C(24)	6456(1)	5803(1)	3793(1)	32(1)
C(25)	6198(1)	5629(1)	3242(1)	30(1)
C(26)	5598(1)	5003(1)	3128(1)	26(1)
C(27)	3697(1)	4073(1)	3121(1)	27(1)
C(28)	3181(1)	4766(1)	3368(1)	25(1)
C(29)	2927(1)	4793(1)	3938(1)	28(1)
C(30)	2451(1)	5429(1)	4162(1)	32(1)
C(31)	2214(1)	6049(1)	3818(1)	33(1)
C(32)	2465(1)	6032(1)	3253(1)	34(1)
C(33)	2947(1)	5397(1)	3030(1)	31(1)

X-ray crystallographic data for **2-((1*S*,2*S*,3*R*)-3-(benzyloxy)-2-(*tert*-butoxymethyl)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Compound S3.8).**

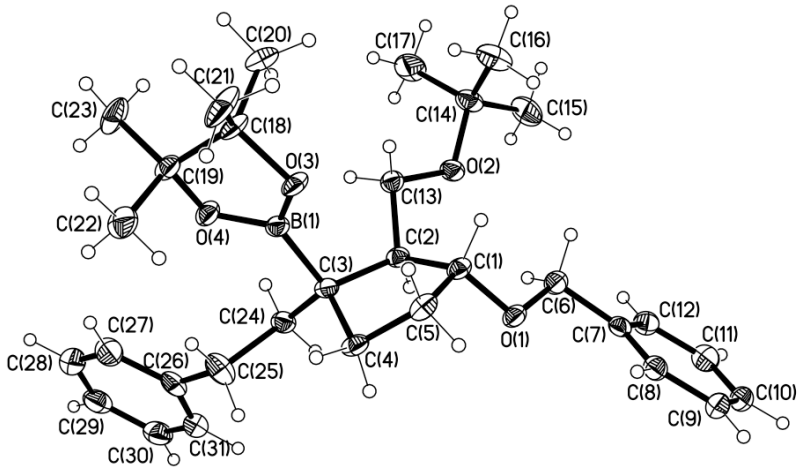


Table S3.12.

Crystal data and structure refinement for **2-((1*S*,2*S*,3*R*)-3-(benzyloxy)-2-(*tert*-butoxymethyl)-1-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Compound S3.8).**

Identification code	$C_{31}H_{45}BO_4$	
Empirical formula	$C_{31}H_{45}BO_4$	
Formula weight	492.48	
Temperature	100(2) K	
Wavelength	1.54178 ≈	
Crystal system	Orthorhombic	
Space group	$Pna2_1$	
Unit cell dimensions	a = 26.2433(11) ≈	a= 90∞.
	b = 17.5408(7) ≈	b= 90∞.
	c = 6.2731(3) ≈	g = 90∞.
Volume	2887.7(2) $\approx^3$	
Z	4	
Density (calculated)	1.133 Mg/m^3	
Absorption coefficient	0.564 mm^{-1}	
F(000)	1072	
Crystal size	0.360 x 0.240 x 0.180 mm^3	

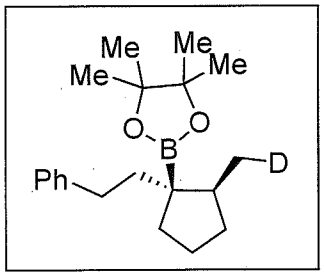
Theta range for data collection	3.030 to 69.934∞.
Index ranges	-31<=h<=31, -21<=k<=18, -6<=l<=7
Reflections collected	22546
Independent reflections	4866 [R(int) = 0.0631]
Completeness to theta = 67.679∞	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7533 and 0.5608
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4866 / 393 / 401
Goodness-of-fit on F^2	1.057
Final R indices [I>2sigma(I)]	R1 = 0.0352, wR2 = 0.0899
R indices (all data)	R1 = 0.0368, wR2 = 0.0912
Absolute structure parameter	0.06(12)
Extinction coefficient	n/a
Largest diff. peak and hole	0.189 and -0.169 e.≈$^{-3}$

Table S3.13.

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (≈^{2}x 10^3) for $C_{31}H_{45}BO_4$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	3636(1)	6170(1)	3554(2)	21(1)
O(2)	3680(1)	4596(1)	7018(2)	22(1)
B(1)	2301(1)	4380(1)	3302(4)	20(1)
C(1)	3375(1)	5467(1)	3104(3)	19(1)
C(2)	3037(1)	5197(1)	4987(3)	18(1)
C(3)	2474(1)	5196(1)	4159(3)	18(1)
C(4)	2499(1)	5778(1)	2310(3)	21(1)
C(5)	3011(1)	5617(1)	1255(3)	22(1)
C(6)	4045(1)	6079(1)	5011(4)	22(1)
C(7)	4374(1)	6783(1)	5004(3)	20(1)
C(8)	4436(1)	7217(1)	3181(4)	22(1)
C(9)	4763(1)	7844(1)	3176(4)	26(1)
C(10)	5036(1)	8028(1)	5001(4)	27(1)
C(11)	4976(1)	7596(1)	6831(4)	28(1)
C(12)	4643(1)	6977(1)	6840(4)	24(1)
C(13)	3210(1)	4446(1)	5971(3)	20(1)
C(14)	3998(1)	3956(1)	7578(4)	26(1)
C(15)	4426(1)	4324(1)	8857(4)	38(1)
C(16)	4212(1)	3580(1)	5589(4)	38(1)
C(17)	3708(1)	3388(1)	8954(5)	39(1)
O(3)	2500(2)	4007(2)	1709(8)	22(1)
C(18)	2256(2)	3251(2)	1658(8)	25(1)

C(19)	1744(2)	3408(2)	2781(6)	22(1)
O(4)	1884(2)	4016(2)	4264(6)	22(1)
C(20)	2606(3)	2722(5)	2866(16)	36(2)
C(21)	2217(8)	3017(12)	-680(20)	43(4)
C(22)	1342(2)	3742(3)	1316(12)	35(1)
C(23)	1527(7)	2728(7)	3990(30)	36(3)
O(3X)	2323(2)	4150(2)	1138(7)	24(1)
C(18X)	2014(2)	3453(2)	974(8)	26(1)
C(19X)	2053(2)	3127(2)	3272(7)	22(1)
O(4X)	2122(2)	3817(2)	4544(5)	18(1)
C(20X)	2218(9)	2932(12)	-710(20)	32(3)
C(21X)	1480(3)	3709(4)	370(12)	36(2)
C(22X)	1582(6)	2724(7)	4070(20)	28(3)
C(23X)	2525(3)	2630(5)	3601(14)	26(2)
C(24)	2109(1)	5444(1)	5954(3)	21(1)
C(25)	1567(1)	5633(1)	5174(4)	33(1)
C(26)	1199(1)	5684(1)	7013(4)	27(1)
C(27)	842(1)	5110(1)	7365(4)	32(1)
C(28)	530(1)	5128(1)	9155(5)	36(1)
C(29)	566(1)	5715(1)	10595(4)	32(1)
C(30)	912(1)	6299(1)	10249(4)	32(1)
C(31)	1223(1)	6281(1)	8467(4)	29(1)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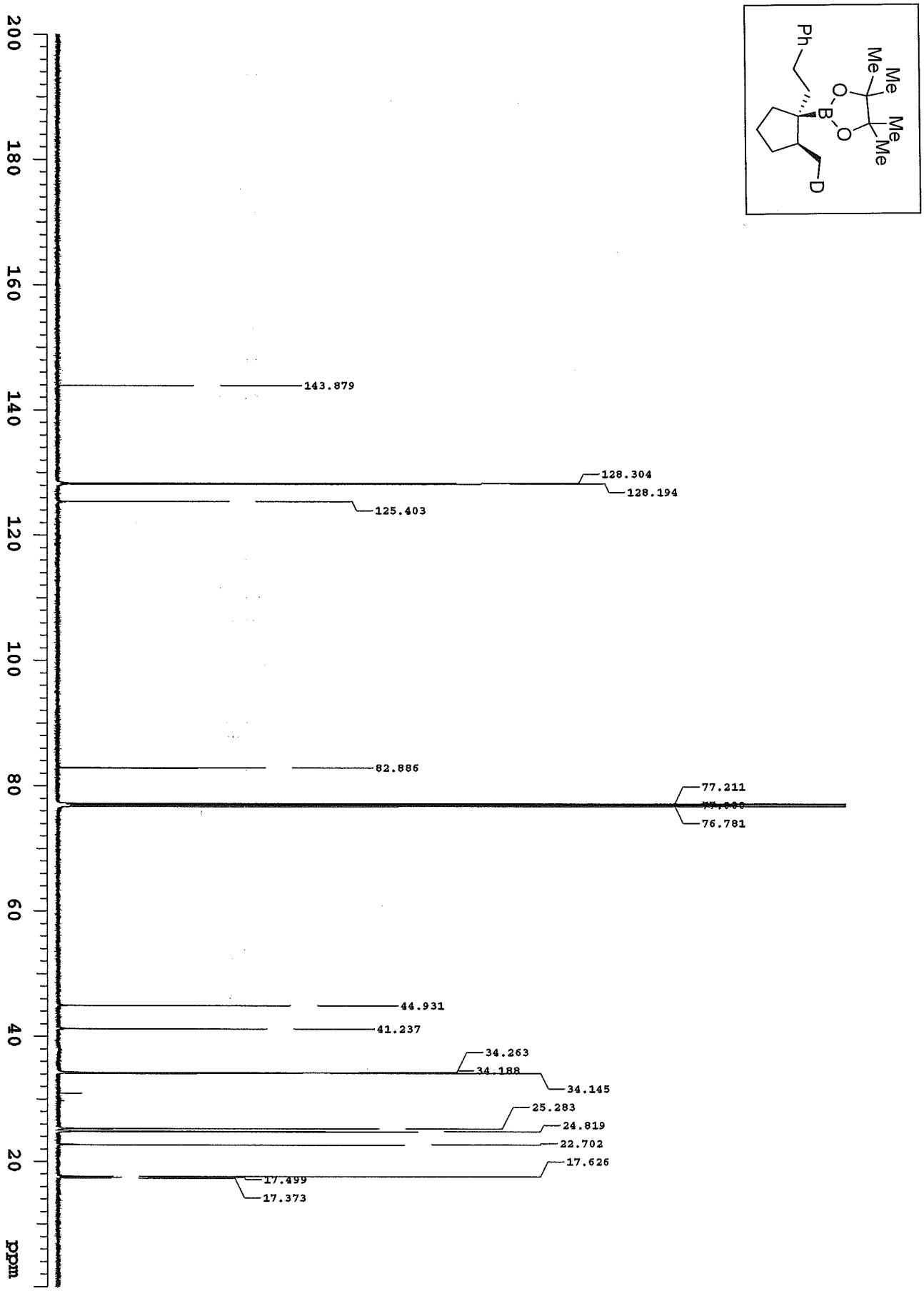
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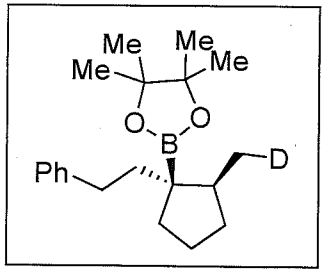
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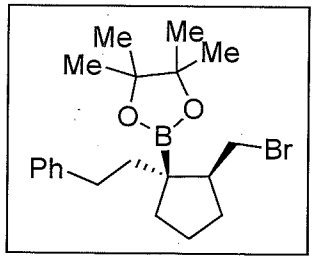
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1.85
1.14
1.02
2.94
12.11

Ph
Me
Me
Me
Me
O
B
O
Br

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120
100
80
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40
20
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77.000
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35.716
33.870
32.226
25.110
24.825
22.358

Chapter 4

Total Synthesis of Natural Product Arenolide

4.1 Introduction

Arenolide, a fourteen-membered macrolide, was isolated from the methanolic extract of a specimen of *Dysidea species* from Palau. Faulkner and coworkers[1] determined its chemical structure through the analysis of NOESY data, which was published in 1998. However, neither the relative configuration of the alcohols at carbon 19 and carbon 21 was clear, nor was the absolute configuration. Arenolide demonstrated relatively low cytotoxicity against HCT human colon carcinoma cells (IC_{50}: 21 mM) and A2780 human ovarian carcinoma cells (IC_{50}: 9.8 mM). Based on the fact that macrolides had never been reported to be isolated from *Dysidea specices* before, Faulkner and coworkers proposed that arenolide might be secreted by other organisms and then absorbed by sponges nearby.

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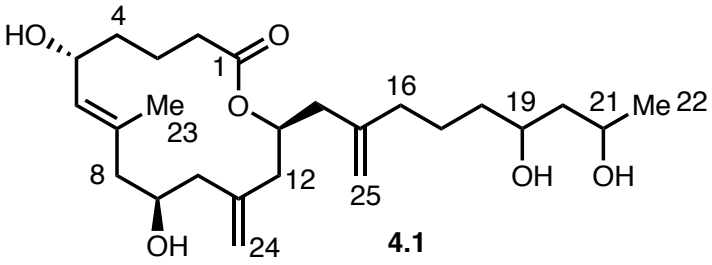
[1] Lu, Q.; Faulkner, D. J. *J. Nat. Prod.* **1998**, *61*, 1096-1100.

Scheme 4.1 Chemical Structure of Arenolide



4.1
Arenolide

While there is no reported total synthesis of Arenolide, Dr. Aaron Cullen and Dr. Carolynn Arpin in Professor Sammakia's group attempted its preparation.[2] They envisioned that the fourteen-membered ring can be cyclized enantioselectively through an intramolecular vinylogous aldol[3] reaction from advanced intermediate **4.3**, which could be constructed from methyl ketone **4.4** and aldehyde **4.5** through a 1,5 *anti*-aldol reaction. To make the synthesis more flexible and modifiable, they simplified the fragment **4.5** into much simpler aldehyde **4.6**. In their model study, even though fourteen-membered cyclized products were detected from mass spectrometry, they could not isolate the desired isomer, let alone determine the accurate yield or diastereoselectivity.

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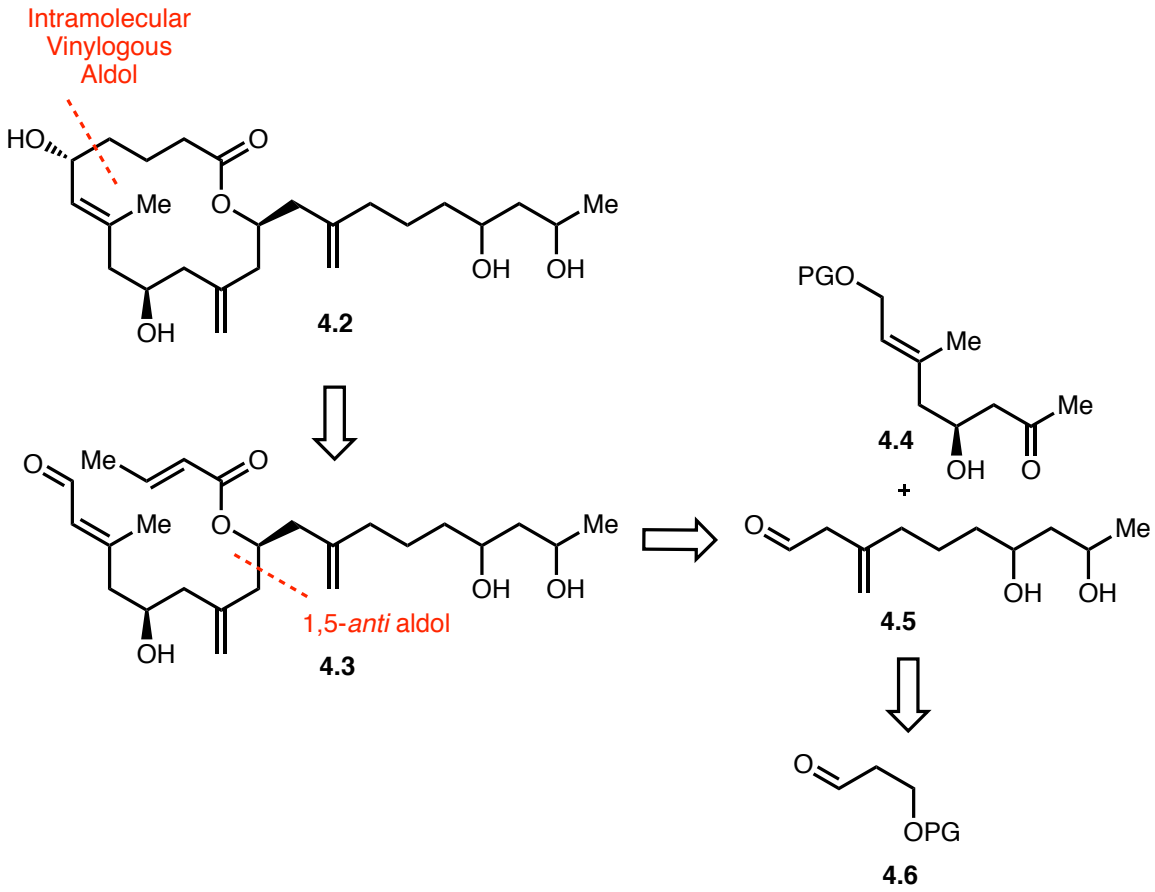
[2] Arpin, C. C. (2011) Cross-Metathesis of Electron-Deficient Polyenes and Studies Toward the Total Synthesis of Arenolide (PhD's thesis). Retrieved from ProQuest Dissertations and Theses database. (UMI No. 3507956)

[3] Abramite, J. A.; Sammakia, T. *Org. Lett*. **2007**, *9*, 2103-2106.

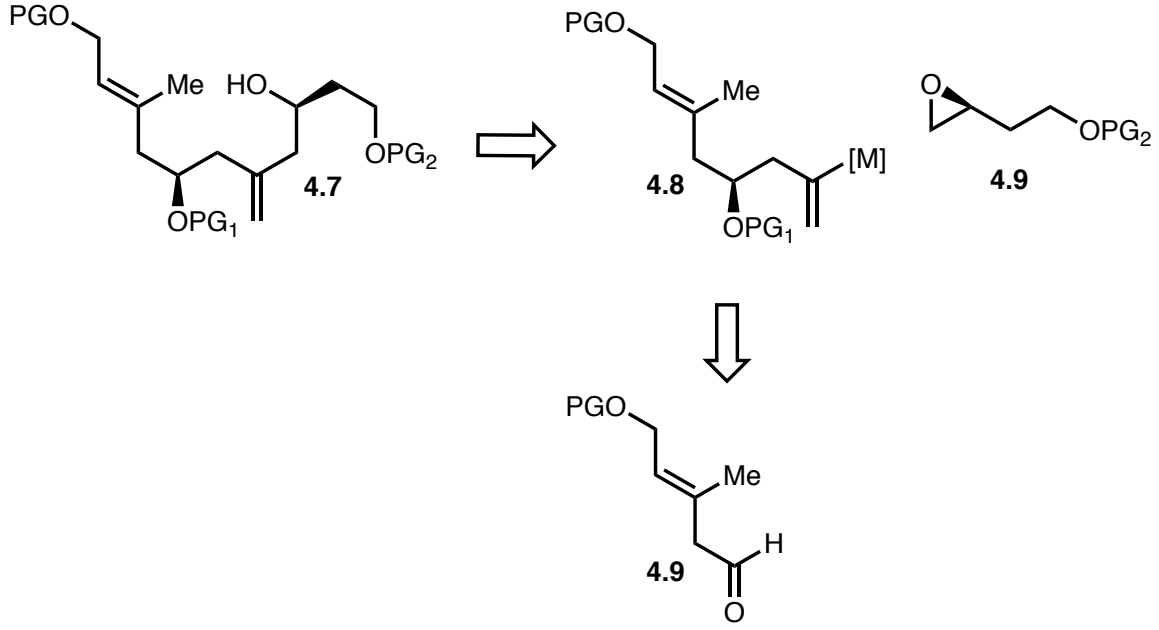
Scheme 4.2 Original Retrosynthesis of Arenolide Proposed by Sammakia and Coworkers



To tackle the low diastereoselectivity issue, the Sammakia team devised a second-generation synthesis towards arenolide. Instead of employing 1,5 *anti*-aldol reaction, they attempted to apply vinyl metal **4.8** in an addition to an enantioenriched

epoxide **4.9**. However, no matter how hard they tried (vinyl lithium,[4] vinyl magnesium bromide[5]), they never obtained the epoxide-opened product **4.7**.

Scheme 4.3 Second Generation Approach to Arenolide by Sammakia and Coworkers



To address this problem, they examined a Suzuki coupling reaction between vinyl iodide **4.10** and 1,2-bis(boronic) ester **4.11**, and then oxidized the secondary boronic ester

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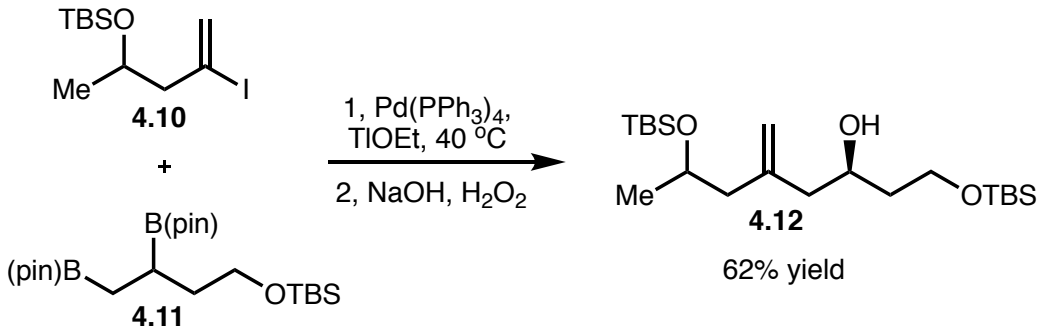
[4] (a) Lipshutz, B. H.; Koerner, M.; Parker, D. A. *Tetrahedron Lett.* **1987**, *28*, 945-948. (b) Pattenden, G.; González, M. A.; Little, P. B.; Millan, D. S.; Plowright, A. T.; Tornos, J. A.; Ye, T. *Org. Bio. Chem.* **2003**, *1*, 4173-4208.

[5] (a) Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F. F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem. Int. Ed.* **2003**, *42*, 4302-4320. (b) Ren, H.; Krasovskiy, A.; Knochel, P. *Org. Lett.* **2004**, *6*, 4215-4217.

into an alcohol. In this manner, the enantioenriched homoallylic secondary alcohol **4.12** was furnished in 62% yield. However, when this methodology was applied with the substrate for the synthesis of arenolide, no desired product was obtained.

Scheme 4.4 Pd-Catalyzed Cross Coupling of 1,2-Bis(boronic) Esters and Vinyl Iodide



4.2 Background

Recently our group developed a series of robust methods to build homoallylic/homobenzylic[6] (Scheme 4.5) and allylic[7]/benzylic[8] (Scheme 4.6) secondary boronic esters in an enantioselective fashion. As shown below, the mono-substituted terminal alkene could undergo catalytic enantioselective diboration with a phosphoamidite derivative as the chiral ligand to afford 1,2-bis(boronic) ester **4.14**. In the

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[6] Mlynarski, S. N.; Schuster C. H.; Morken J. P. *Nature* **2014**, *505*, 386-390.

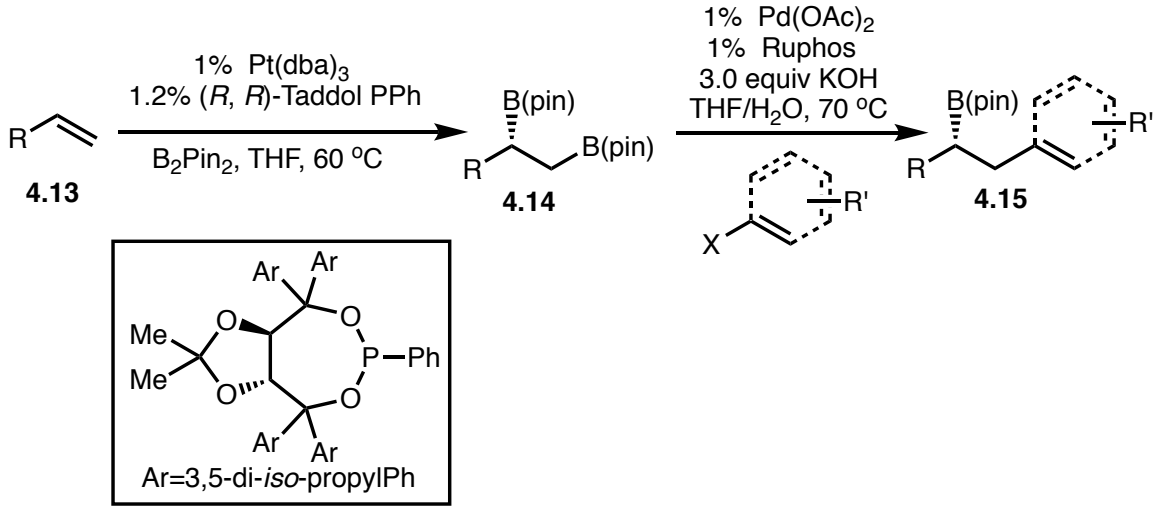
[7] Potter, B.; Szymaniak, A. A.; Edelstein, E. K.; Morken. J. P. *J. Am. Chem. Soc.* **2014**, *136,* 17918-17921.

[8] Sun, C.; Potter B.; Morken J. P. *J. Am. Chem. Soc.* **2014**, *136,* 6534-6537.

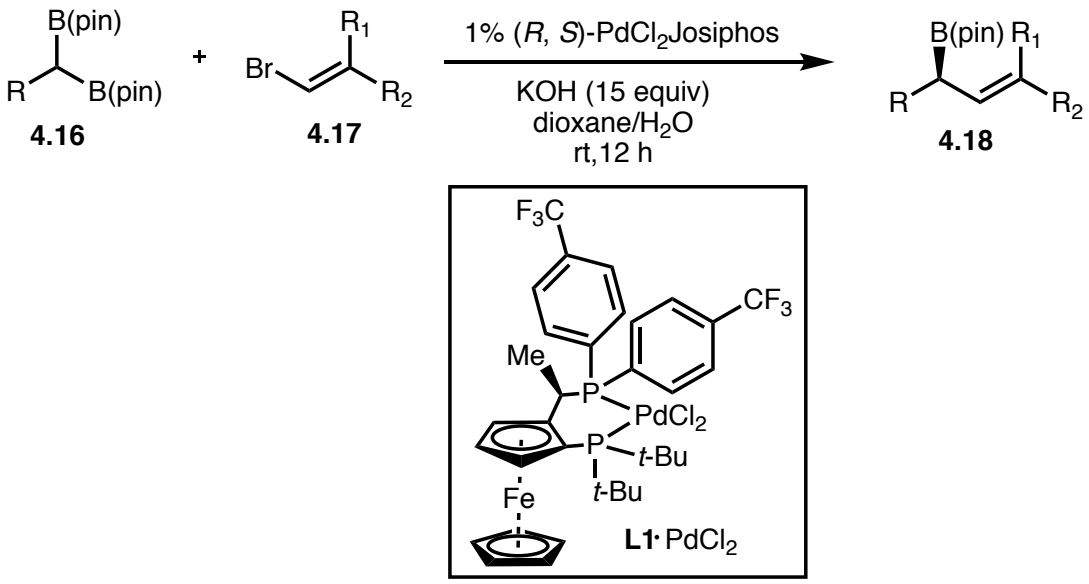
presence of the secondary boronic ester, only the primary one was coupled with vinyl halides or aryl halides to deliver a homoallylic/homobenzylic boronate **4.15** in good yields.

Meanwhile, our group also established that with the combination of Josiphos and $PdCl_2$ (**L1**•$PdCl_2$), 1,1-diboryl alkanes and tri-substituted alkenyl halides could be merged together through Suzuki coupling reaction, delivering an enantioenriched secondary allylic boronic ester **4.18** (Scheme 4.6).

Scheme 4.5 Diboration and Cross-Coupling Reaction



Scheme 4.6 Suzuki Coupling Reaction between 1,1-Diboranes and Alkenyl Halides



More recently, our group developed a transition metal-free version of the catalytic enantioselective diboration of terminal alkenes.[9] Subsequently, the allylic secondary boronate was then oxidized to alcohol **4.20** in a stereoretentive fashion. This transformation was achieved with pseudoenantiomeric glycols 6-*tert*-butyldimethylsilyl-1,2-dihydroglucal (TBS-DHG) and dihydrorhamnal (DHR), which could be obtained readily from commercial available cheap starting material D-glucal and L-rhamnal. Through mechanistic studies, 1,2-bonded B_2(TBS-DHG)$_2$ was believed to be the reactive intermediate.

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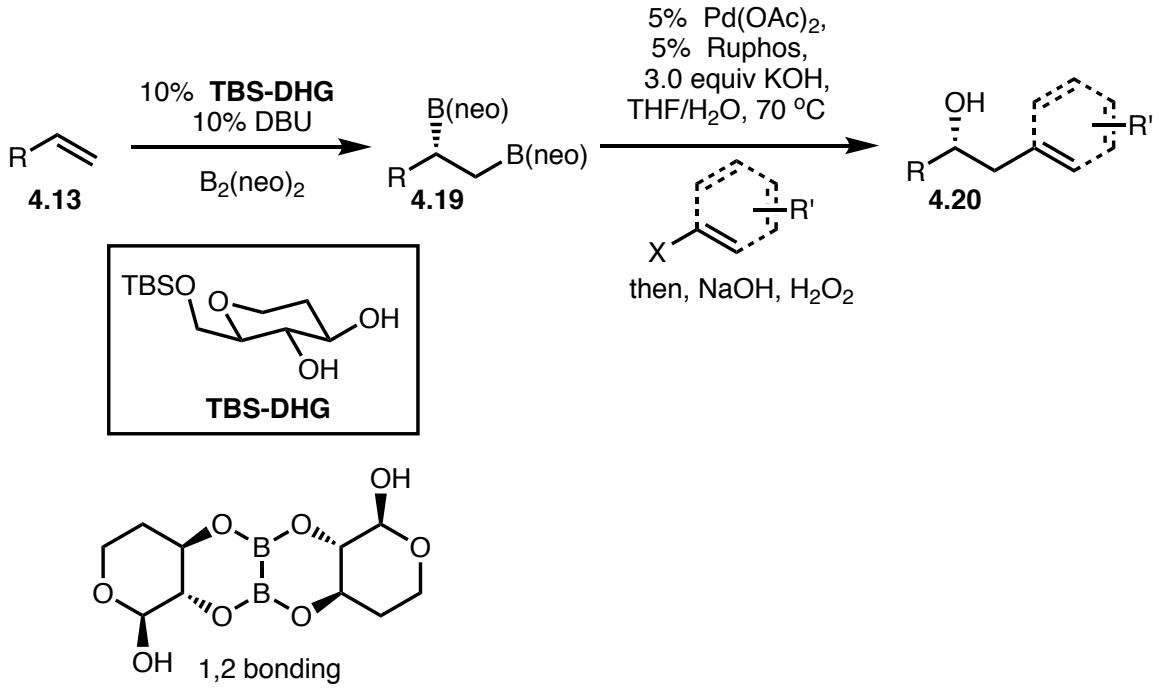
[9] Fang, L.; Yan, L.; Haeffner, F.; Morken, J. P. *J. Am. Chem. Soc.* **2016**, *138*, 2508-2511.

Scheme 4.7 Synthesis of Homoallylic Alcohol Catalyzed by a Carbohydrate



Since boronic esters can be easily oxidized, they are regarded as masked alcohols. We wondered whether these catalytic methodologies could be well knitted into the total synthesis of natural product Arenolide.

Pursuing this proposal, this project was initiated by previous group member Dr. Mlynarski, and Dr Chunrui Sun, who both made significant contributions to this total synthesis. However, the two methodologies (Scheme 4.6 and 4.7) mentioned above were not available approaches and my research has focused on an alternate route.

4.3 Total Synthesis of Natural Product Arenolide

When we revisited Arenolide, we decided to modify the original synthetic route to cyclize the fourteen-membered ring by selective macrolactonization. Also, we altered routes to incorporate updated methodologies that reduce the use of toxic reagents and make the synthesis more concise.

Demonstrated below is the retrosynthetic analysis of Arenolide. We envisioned that the fourteen-membered ring could be cyclized by Yamaguchi lactonization.[10] The precursor for the cyclization step could be accessed from the Suzuki coupling reaction between 1,2-bis(boronate) **4.22** and alkenyl chloride **4.23**.[11] The fragment A (**4.22**) was then traced back to another 1,2-diboron **4.24**, which was allowed to react with 1,1-disubstituted alkenyl bromide **4.25**. To obtain 1,2-bis(boronic) ester **4.24**, readily accessible geminal bis(boronate) **4.26** was proposed to cross couple with trisubstituted alkenyl bromide **4.27** in a catalytic and enantioselective manner.[12]

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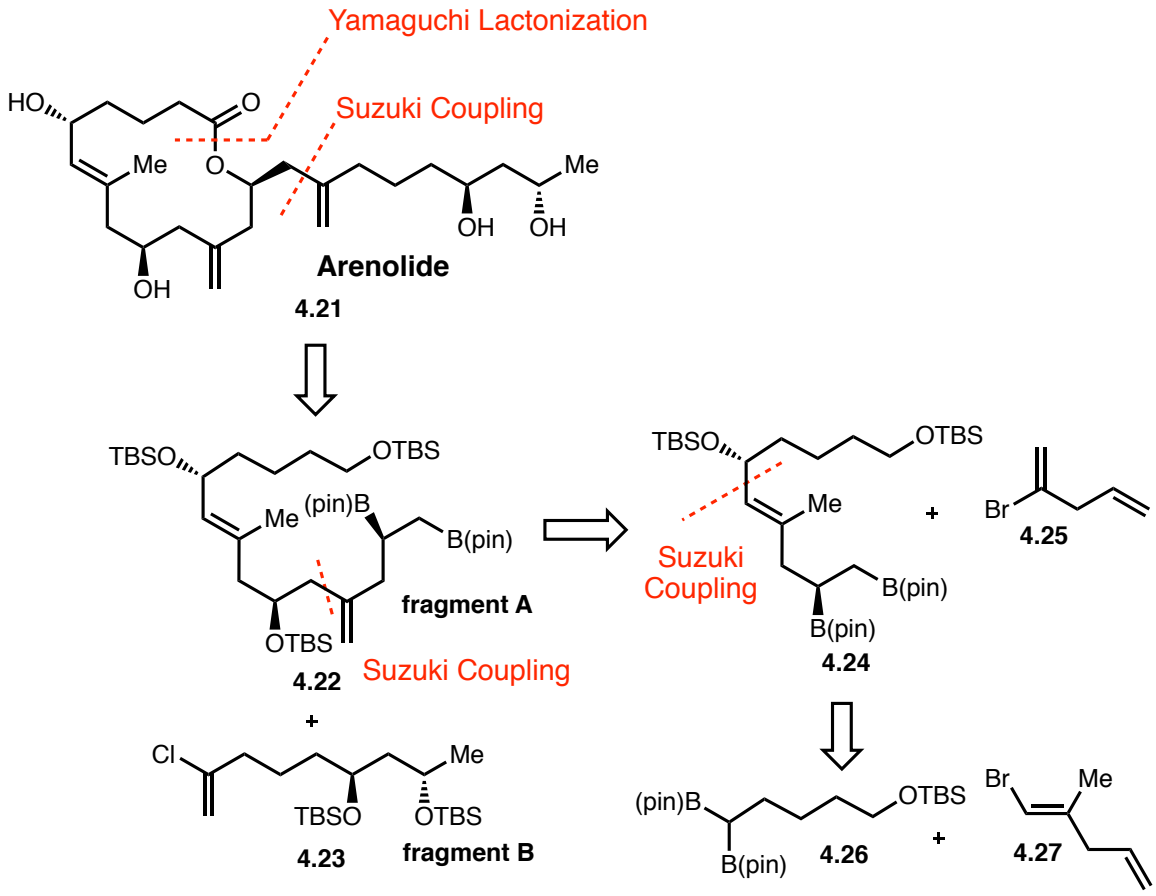
[10] Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989-1993.

[11] Mlynarski, S. N.; Schuster C. H.; Morken J. P. *Nature* **2014**, *505*, 386-390.

[12] Potter, B.; Szymaniak, A. A.; Edelstein, E. K.; Morken. J. P. *J. Am. Chem. Soc.* **2014**, *136,* 17918-17921.

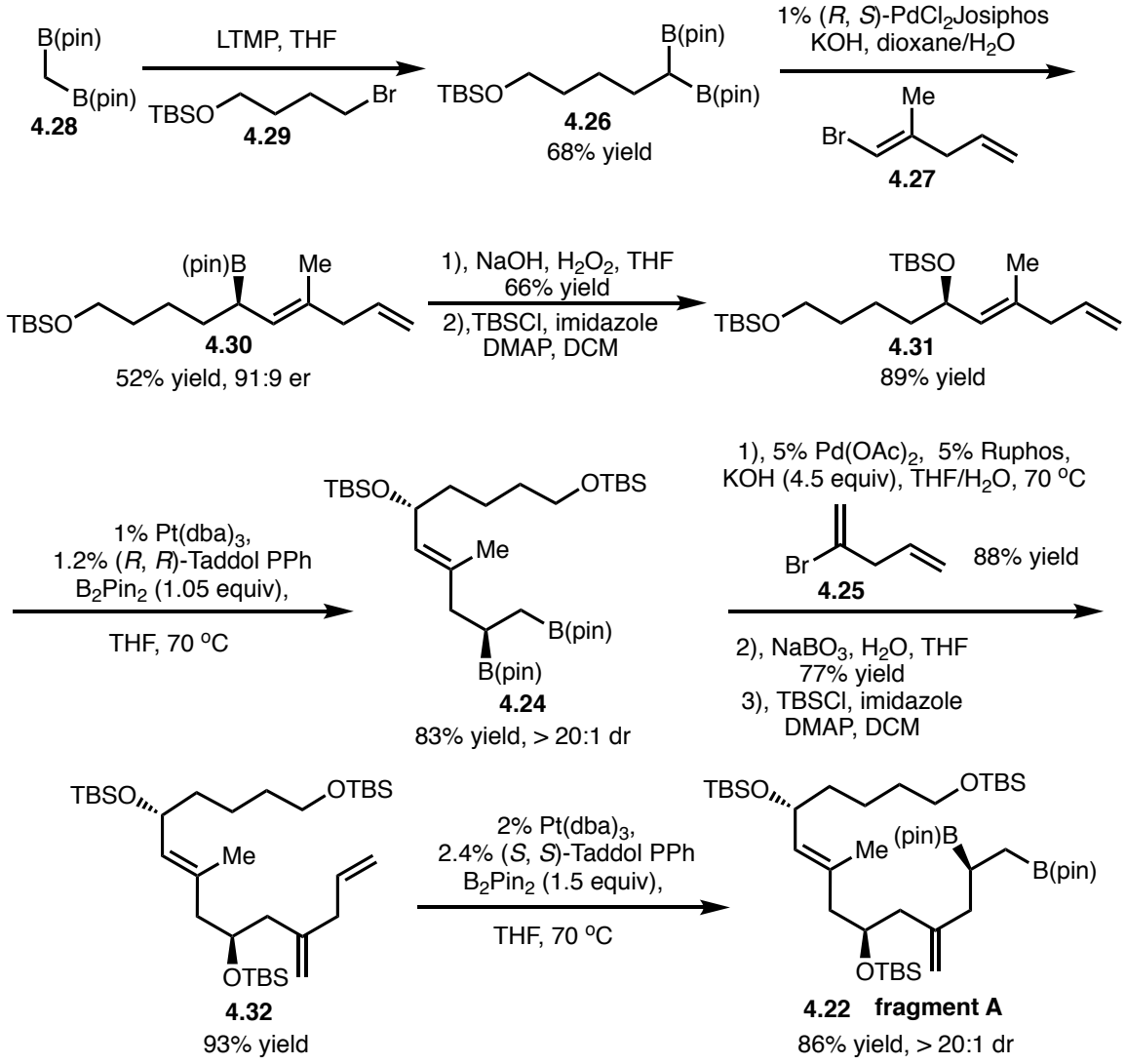
Scheme 4.8 Retrosynthetic Analysis of Arenolide



We began our synthesis journey with readily available 1,1-diboryl methane **4.28**. After deprotonation of the acidic methylene carbon, alkyl halide **4.29** was added to furnish the alkylated product **4.26**. The geminal bis(boronic) ester **4.26** was then allowed to couple with tri-substituted alkenyl bromide **4.27** in the presence of catalytic amount **L1**•$PdCl_2$ to afford allylic boronic ester **4.30** with high enantioselectivity. The possible byproducts of Heck reaction, as well as possible byproducts from alkene-isomerization, were not observed. The boronic ester **4.30** was then converted into an alcohol (not

shown), and protected with silyl ether to deliver diol **4.31**. With the terminal alkene obtained, we were well positioned to carry out the enantioselective diboration regioselectively to give the 1,2-di(boronate) **4.21** in a good yield and with excellent diastereoselectivity. A Suzuki coupling between 1,1-disubstituted alkenyl bromide **4.25** and 1,2-bis(boronic) ester **4.21** was then performed smoothly to give enantioenriched secondary boronic ester in 88% yield. The boronate was then oxidized into the desired alcohol, followed by protection as a silyl ether to afford triene product **4.32** in a good yield. This terminal alkene **4.32** was then subjected to the platinum catalyzed enantioselective diboration condition to deliver 1,2-bis(boronic) ester **4.22** in 86% yield with over 20:1 diastereoselectivity.

Scheme 4.9 Forward Synthesis of Fragment A



The alkenyl coupling partners **4.25** and **4.27** (shown in Scheme 4.9) are not commercially available and were synthesized in the lab. We envisioned that both fragments could be derived from the same starting material 1-penten-4-yne (**4.35**). As

demonstrated in Scheme 4.10 equation 1, cross-coupling between ethynyl magnesium bromide (**4.33**) and allyl bromide **4.34** was carried out.[13] Based on the ^{1}H NMR, the desired product 1-penten-4-yne **4.35** was formed. However, due to its low boiling point (41 °C), isolation by column chromatography was not practical as the pentane solvent has a boiling point of 36 °C, which is very similar to the product. Instead, 1-penten-4-yne **4.35** was distilled out from the reaction mixture, and sealed in a flask with a rubber septum in the freezer. However, due to the extreme volatility of this compound, we were unable to successfully store it.

Then bromination-based synthetic route in equation 2 in Scheme 4.10 was evaluated. However, the *E/Z* configuration ratio of the desired product stereoisomer of alkenyl bromide **4.37** to the minor compound was only 4:1 after the elimination step, which was unsatisfactory for the synthetic utilization.[14]

After searching resources again, we considered 1-penten-4-yne **4.35** from GFS as a relatively cheap (10 g/ 106.6 $) starting material. With this commercially available starting material in hand, we easily synthesized the tri-substituted alkene **4.27** through zirconium-catalyzed hydroalumination reaction followed by trapping with *N*-bromosuccinimide to deliver the desired product **4.27** in a relatively good yield.

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[13] Zhu, G.; Negishi, E. *Chem.-Eur. J.* **2008**, *14*, 311-318.

[14] Taber, D. F.; Sikkander, M. I.; Storck, P. H. *J. Org. Chem.* **2007**, *72*, 4098-4101.

To obtain diene fragment **4.25**, copper-catalyzed cross coupling[15] between allyl bromide **4.39** and vinyl Grignard **4.40** was attempted. However, the reaction was not efficient enough and afforded product **4.25** in more than 10% yield. Delightfully, the methodology developed by Hoveyda and coworkers [16] lighted our synthesis. Nickel-catalyzed hydroalumination at the internal position, followed by trapping with *N*-bromosuccinimide worked beautifully for our substrate, providing desired alkenyl bromide **4.25** in 38% yield. This yield might due to the loss of some fractions during isolation, as product **4.25** has a low boiling point around 100 °C.

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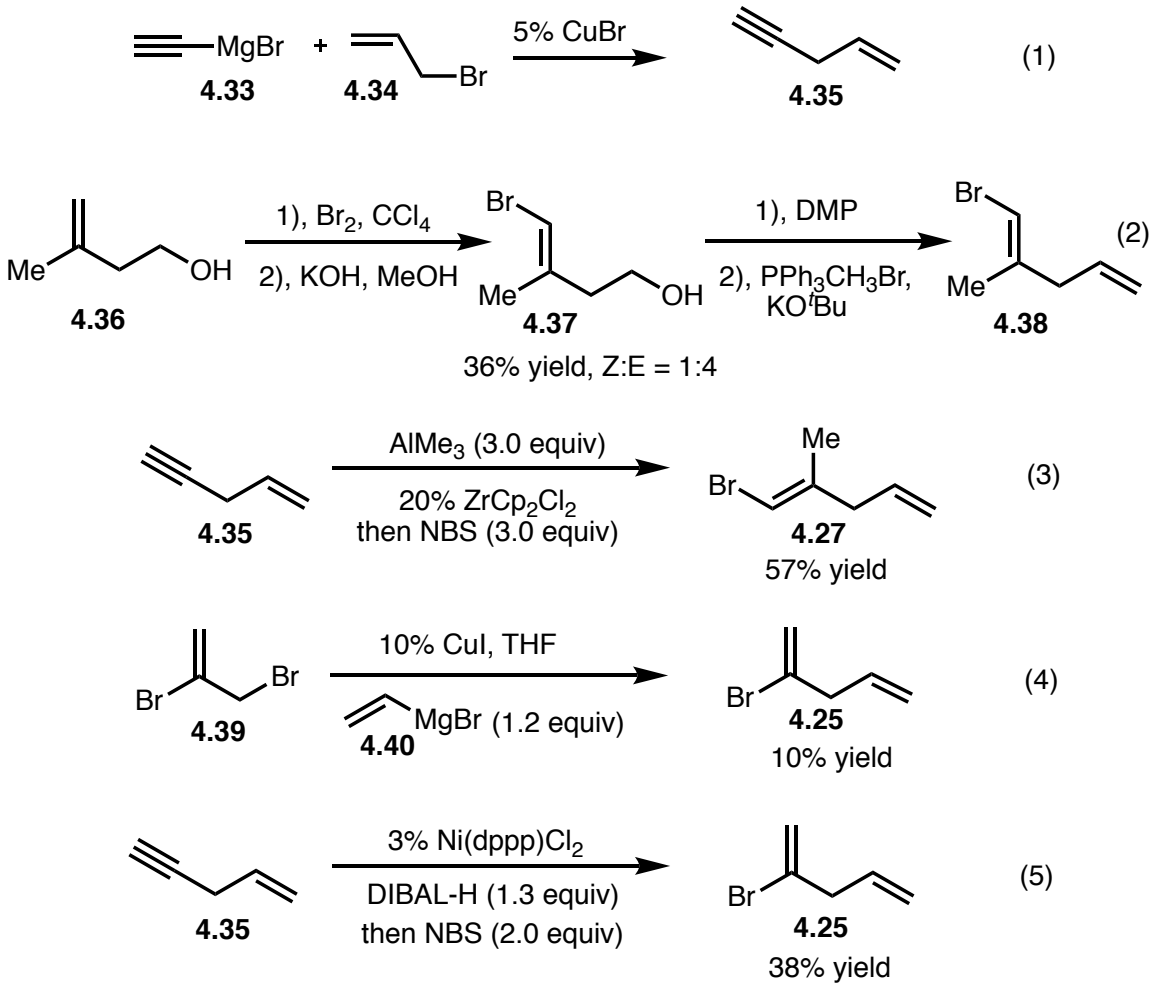
[15] Watanabe, K.; Minato, H.; Murata, M.; Oishi, T. *Heterocycles* **2007**, *72*, 207-212.

[16] Gao, F.; Hoveyda A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10961-10963.

Scheme 4.10 Synthesis of Vinyl Bromide Fragments



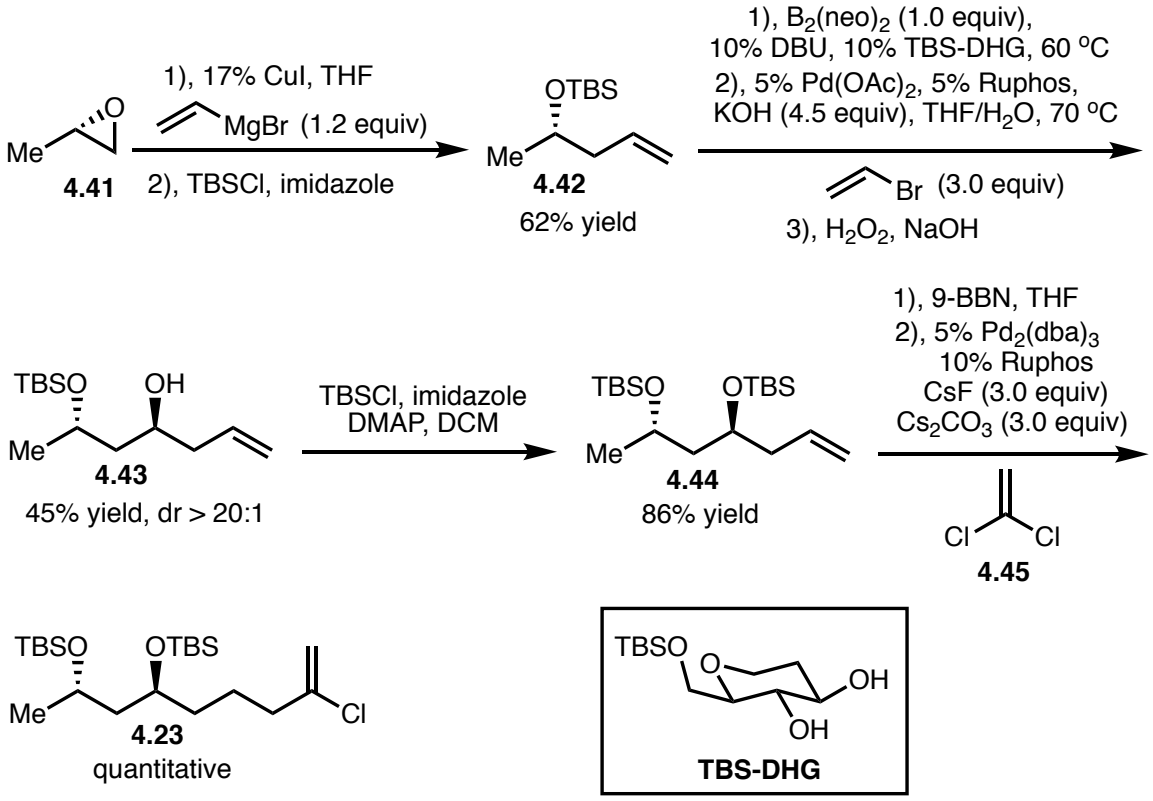
The synthesis of alkenyl chloride fragment B was more straightforward. Under the catalysis of copper iodide, vinyl magnesium bromide could open enantioenriched epoxide **4.41** to deliver a secondary alcohol[17] (not shown), which was then protected with silyl chloride to deliver protected homoallylic alcohol **4.42** in 62% yield. The

[17] Mlynarski, S. N.; Schuster C. H.; Morken J. P. *Nature* **2014**, *505*, 386-390.

terminal alkene **4.42** could also undergo enantioselective diboration under the catalysis of TBS-DHG to establish 1,2-bis(boronate) (not shown). The primary boronic ester was then coupled with vinyl bromide in the presence of vicinal secondary boronate, the latter was then oxidized into an alcohol to deliver 1,3-*trans* diol product **4.43**. The secondary alcohol **4.43** was protected with a silyl group to afford compound **4.44**. Hydroboration of the terminal alkene **4.44** resulted in the formation of a primary organoborane (not shown), which could then undergo Suzuki coupling[18] with 1,1-dichloroethene to furnish vinyl chloride fragment B in a good yield.

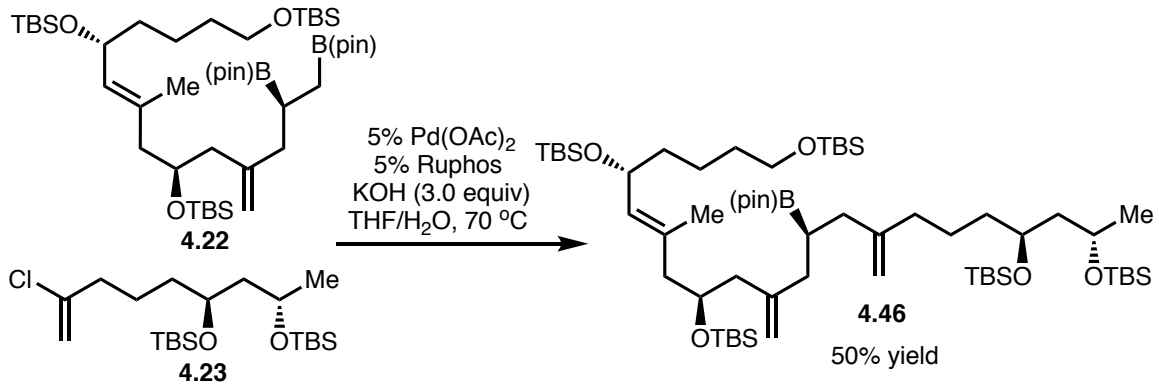
[18] Liron, F.; Fosse, C.; Pernolet, A.; Roulland, E. *J. Org. Chem.*, **2007**, *72*, 2220-2223.

Scheme 4.11 Synthesis of Alkenyl Chloride Fragment B



With fragment A (**4.22**) and fragment B (**4.23**) in hand, we next explored to engage the two halves together. The yield for the cross coupling was 50%, which was respectable considering the presence of multiple functional groups involved. We hypothesized that β–H elimination and palladium-involved deborylation were the two major side reactions, which lead to terminal alkenes observed as the byproducts.

Scheme 4.12 Cross-Coupling to Engage Fragment A and Fragment B Together



With advanced intermediate **4.46** in hand, we proceeded to selectively deprotect the primary alcohol to afford compound **4.47**. Among the conditions we examined, this 1N hydrochloric acid in THF reaction condition offered the best yield, even though this reaction was sensitive to reaction time (12 hours) and temperature (0 °C). The alcohol was then oxidized into aldehyde[19] (not shown), which was converted into carboxylic acid[20] **4.48** in a good yield. The boronic ester in **4.48** was then unmasked through oxidation, and the generated alcohol esterified with carboxylic acid intramolecularly[21] to

---

[19] (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155-4156. (b) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277-7287.

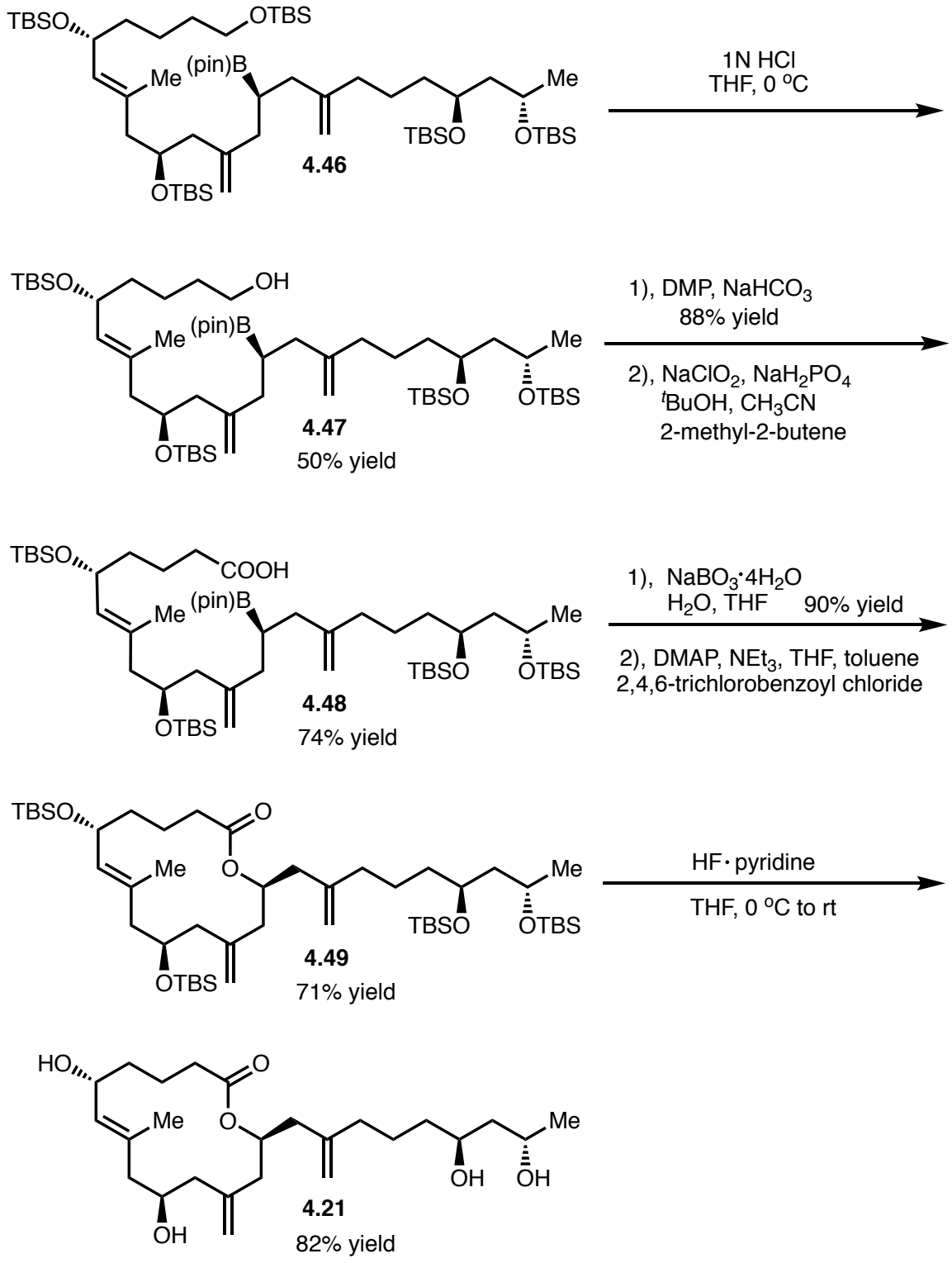
[20] (a) Lindgren, B. O.; Hilsson, T. *Acta Chem. Scand.* **1973**, *27*, 888-890. (b) Kraus, G. A.; Taschner, M. J. *J. Org. Chem.* **1980**, *45*, 1175-1176. (c) Kraus, G. A.; Roth, B. *J. Org. Chem.* **1980**, *45*, 4825-4830. (d) Bal, B. S.; Childers, W. E., Jr.; Pinnick, H. W. *Tetrahedron* **1981**, *37*, 2091-2096.

[21] Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989-1993.

afford the fourteen-membered ring **4.49** exclusively. After global deprotection,[22] the desired product **4.21** was delivered in 82% yield.

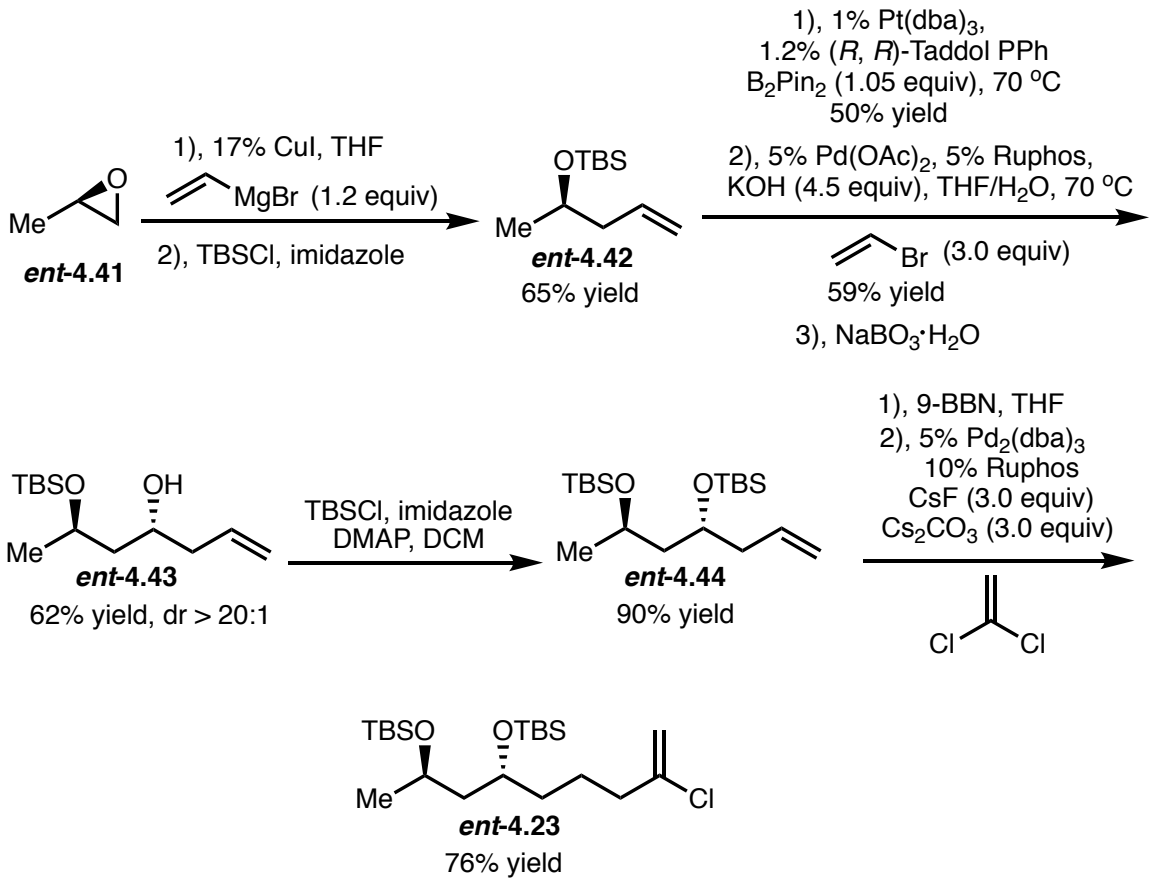
[22] Paterson, I.; Britton, R.; Delgado, O.; Gardner, N. M.; Meyer, A.; Naylor, G. J.; Poullennec, K. G. *Tetrahedron* **2010**, *66*, 6534-6545.

Scheme 4.5 Late Stage Functional Group Manipulation of Isomer **1**



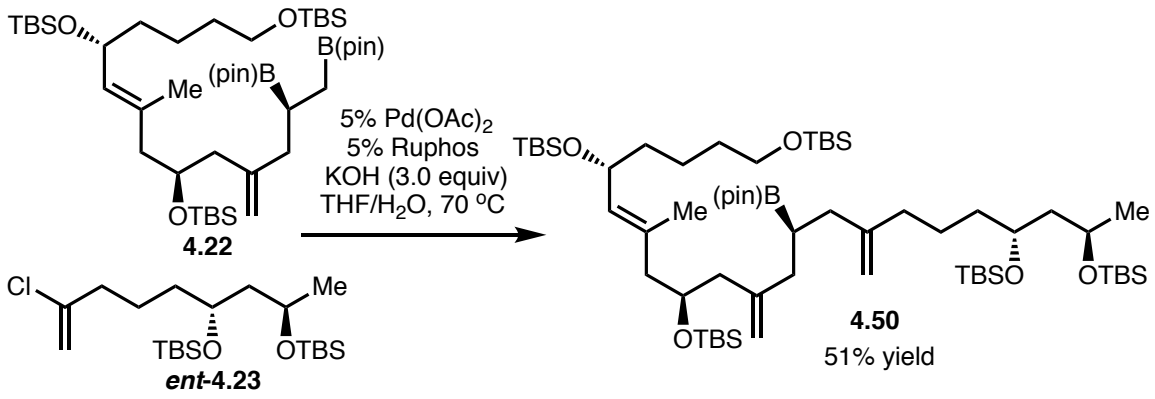
The route to synthesize the enantiomer of fragment B **4.23** is very similar to the strategy mentioned above, with the exception of using the enantiomer of the epoxide **4.41** and inducing the opposite stereocenter in the catalytic enantioselective diboration step. Starting from commercial available (*R*)-propylene oxide, which was opened by vinyl magnesium bromide from the less hindered side to deliver the homoallylic alcohol (not shown). The alcohol was then protected with silyl ether to provide *ent*-**4.42**. Platinum-catalyzed enantioselective diboration of terminal alkene with *ent*-**4.42** then delivered 1,2-bis(boronic) ester (not shown) in 50% yield, which then cross coupled with vinyl bromide to tether an alkene moiety. The untouched secondary boronate was then oxidized to alcohol to give *ent*-**4.43** and protected with silyl ether to deliver 1,3-*trans* diol *ent*-**4.44**. Hydroboration of terminal alkene *ent*-**4.44** with 9-BBN dimer afforded primary alkyl borane, which underwent cross coupling with 1,1-dichloroethene to furnish the enantiomer of fragment B *ent*-**4.23**.

Scheme 4.14 Construction of Enantiomer of Alkenyl Chloride Fragment B



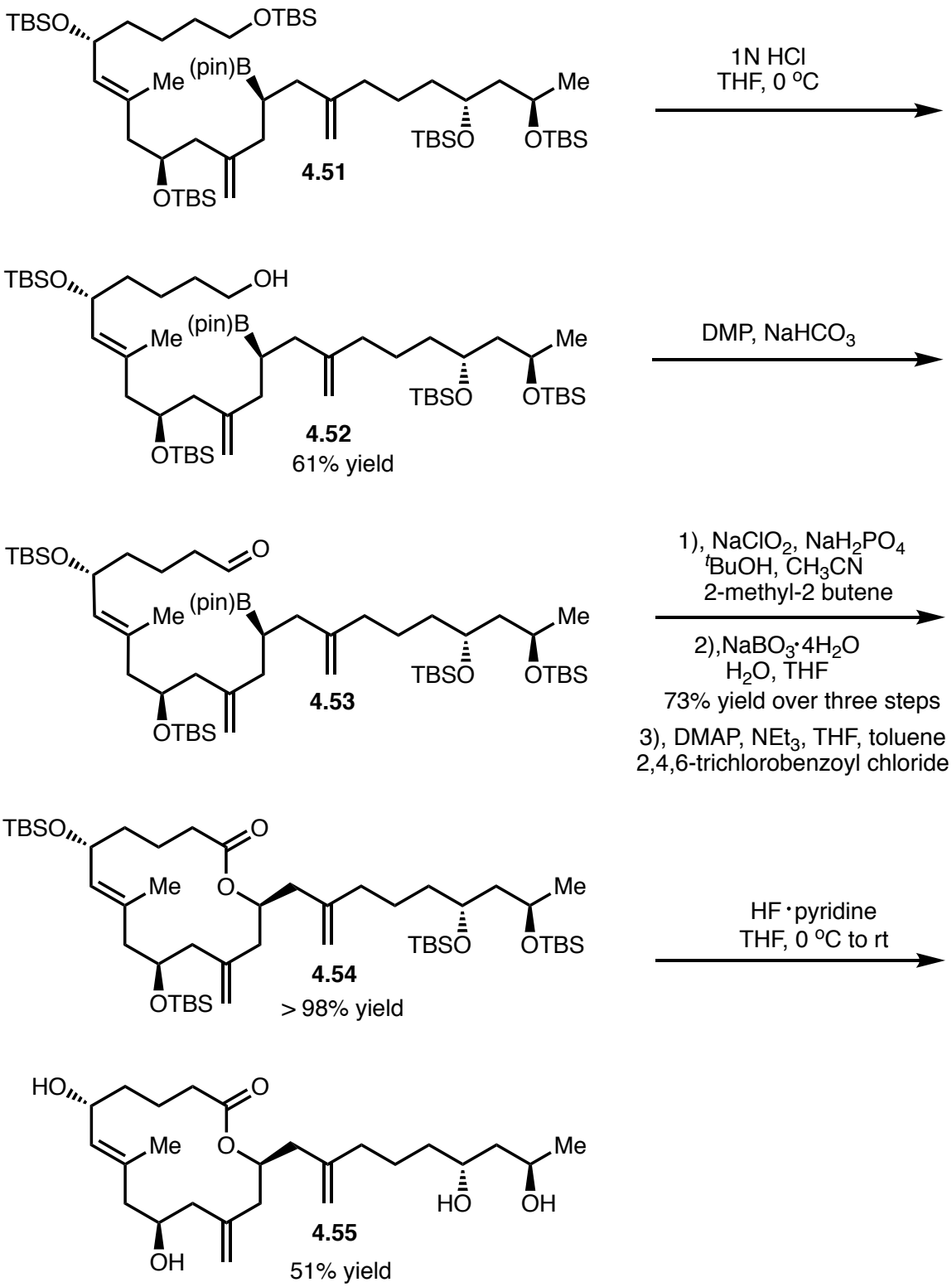
The palladium/Ruphos-catalyzed Suzuki coupling between fragment A (**4.22**) and *ent*-fragment B (*ent*-**4.23**) with Ruphos as the ligand went very smoothly to deliver the advanced synthetic intermediate **4.50** in 51% yield.

Scheme 4.15 Cross-Coupling to Piece Fragment A and *ent*-Fragment B Together



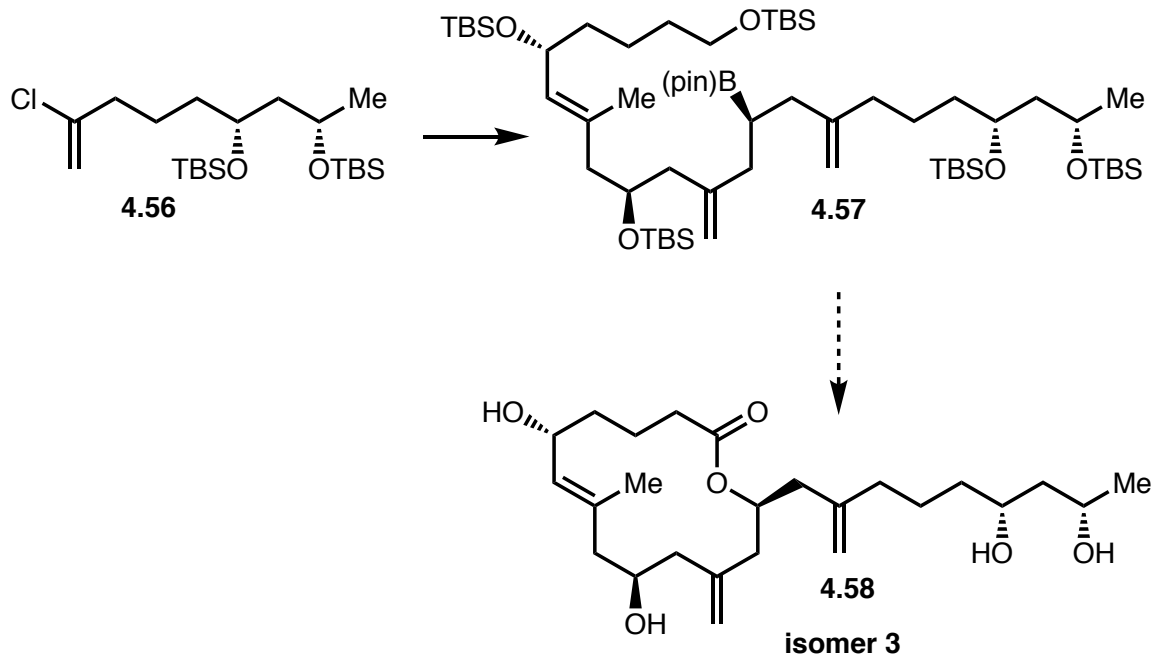
With the core structure **4.51** in hand, we moved on to selectively deprotect the primary alcohol among the five silyl ether protected ones to deliver compound **4.52**. The exposed alcohol was then converted to aldehyde through Dess-Martin oxidation, which was further oxidized to carboxylic acid (not shown) through Pinnick oxidation. The masked boronic ester was then unveiled by oxidation. The total yield of these three steps was 73%. Yamaguchi lactonization was then carried out to construct the fourteen-membered ring core structure **4.54** in a very efficient way. After deprotecting the silyl ether globally, isomer **2** (compound **4.55**) was accomplished in 51% yield.

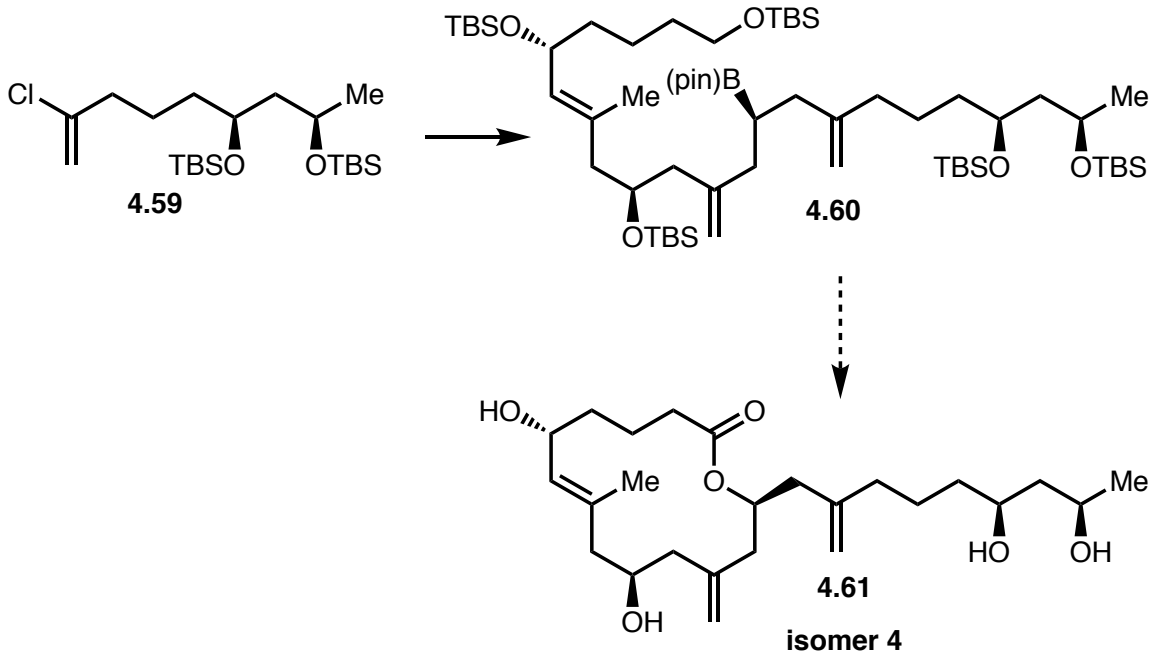
Scheme 4.16 Late Stage Functional Group Manipulation of Isomer **2**



The other two diastereomers (**4.56** and **4.59** as shown in Scheme 4.17) of fragment B were also synthesized by applying a very similar strategy, only with different combination of enantioenriched epoxides and catalysts for enantioselective diboration in the sense of chirality. Both alkenyl chloride diastereomers (**4.56** and **4.59**) underwent Suzuki coupling reaction with fragment A to deliver the advanced intermediate **4.57** and **4.60**. However, as far as late stage functional group manipulations went, we did not have enough material to carry forward to the end to obtain **isomer 3** and **isomer 4**.

Scheme 4.17 Attempt to Synthesize **Isomer 3** and **Isomer 4**





4.4 Determination of the Stereostructure of Arenolide among Possible Stereoisomers

The reported ^{13}C NMR data suggests that the alcohols at C19 and C21 position are in a *trans* relationship.

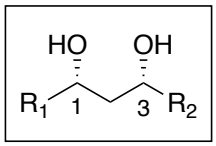
Hoffman and coworkers[23] found the ^{13}C chemical shifts of 1,3-*anti*-diols normally occur upfield by about 4 ppm comparing to that of 1,3-*syn*-diols. This is probably due to the axial substituent of 1,3-*anti*-diols resulting from a hydrogen-bonded cyclic conformation, while the substituents on 1,3-*syn*-diols usually adopts an equatorial

[23] Hoffmann, R. W.; Weidmann, U. *Chem. Ber.* **1985**, *118*, 3980-3992.

position. They also noted that the sum of the two carbinol carbons of *anti*-1,3-diols is usually less than 140 ppm (Table 4.2) and the ^{13}C chemical resonance sum of *syn*-1,3-diols is usually more than 140 ppm. (Data shown in Table 4.1). This theory was later adopted by Brückner and coworkers[24] in assigning the configuration of the 1,3-diol products.

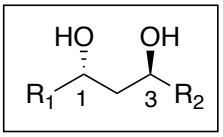
[24] Diehl, J.; Brückner, R. *Eur. J. Org. Chem*. **2017**, 278-286.

Table 4.1. Carbon Chemical Shifts of 1,3-*syn*-Diols



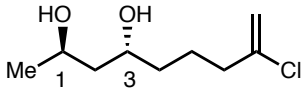
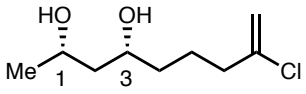
Entry	R_1	R_2	$\delta_{C\text{-}1}$ [ppm]	$\delta_{C\text{-}3}$ [ppm]	Sum [ppm]
1	CH_3	$-CH_2-CH=CH_2$	68.6	71.7	140.3
2	CH_3	$-(CH_2)_3-C(CH_3)=CH_2$	68.8	72.2	141.0
3	CH_3	$-C(CH_3)_2-CH=CH_2$	69.1	79.3	148.4
4	CH_3	$-CH_2CH_2CH_3$	68.5	72.1	140.6
5	CH_3	$-CH_2CH_2CH_2CH_3$	69.3	73.3	142.6
6	*c*Pr	CH_3	78.0	68.8	146.8
7	*i*Pr	CH_3	78.1	69.5	147.6

Table 4.2. Carbon Chemical Shifts of 1,3-*anti*-Diols



Entry	R_1	R_2	δ_{C-1} [ppm]	δ_{C-3} [ppm]	Sum [ppm]
1	CH_3	$-CH_2-CH=CH_2$	65.0	68.0	133.0
2	CH_3	$-(CH_2)_3-C(CH_3)=CH_2$	64.8	68.5	133.3
3	CH_3	$-C(CH_3)_2-CH=CH_2$	65.5	74.4	139.9
4	CH_3	$-CH_2CH_2CH_3$	64.9	68.5	133.4
5	CH_3	$-CH_2CH_2CH_2CH_3$	65.7	69.6	135.3
6	*c*Hex	CH_3	73.5	65.8	139.3
7	*i*Pr	CH_3	74.1	65.8	139.9

Our model studies of substrates **27** and **28** also supported this theory. The sum of ^{13}C chemical shifts of *anti*-1,3-diols is 134.61 ppm (Table 3, entry 1), while for *syn*-1,3-diols, the sum is 141.86 ppm (Table 3, entry 2).

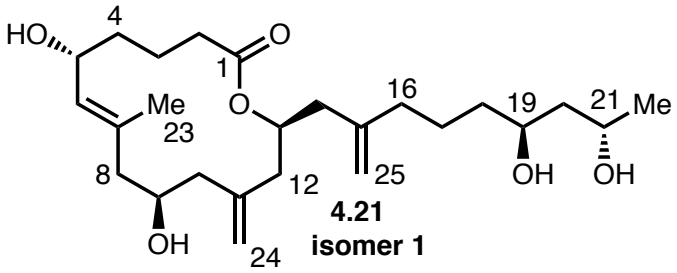
1,3-Diol Substrates	$\delta_{C\text{-}1}$ [ppm]	$\delta_{C\text{-}3}$ [ppm]	Sum [ppm]
	65.61	69.00	134.61
	69.29	72.57	141.86

The reported ^{13}C chemical shifts of arenolide at C19 and C21 are 69.1 and 65.5 ppm respectively. The sum of these two numbers is 134.6 ppm. These data indicated that the 1,3-diols of C19 and C21 in arenolide are in an *anti* relationship.

The ^{1}H and ^{13}C NMR spectra of synthesized isomer **1** (**4.21**) and isomer **2** (**4.55**) were compared with the data collected from the natural product (Scheme 4.19 and Scheme 4.20). We found that isomer **1** matches much better with the reported spectra than isomer **2**, while the latter has two significant differences in chemical shifts in ^{13}C NMR spectra (shown in red in Scheme 4.20). We concluded that isomer **1** is more

consistent chemical structure as the natural product arenolide. Compared with the reported optical rotation number for arenolide ($[\alpha]_D$ +13.0° (*c* 0.64, $CHCl_3$)), the optical rotation number for isomer **1** we synthesized is $[\alpha]_D$ +5.997° (*c* 0.0667, $CHCl_3$). This indicated that isomer **1** resembles the most of the naturally occuring arenolide.

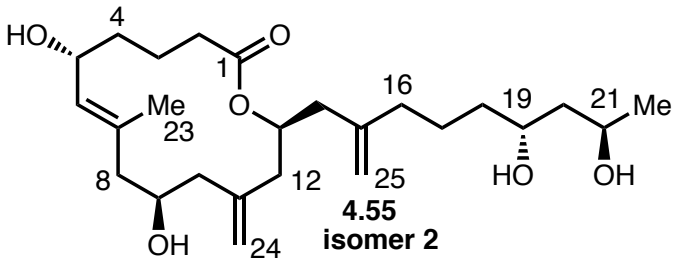
Scheme 4.8 Comparison of the ^1H and ^{13}C NMR Spectra of **Isomer1** (**4.21**) and the Natural Product Arenolide



	δ_H		δ_C	
	Natural (400 MHz)	Synthetic (600 MHz)	Natural (100 MHz)	Synthetic (150 MHz)
1			172.5	172.42
2	2.12, m 2.33, m	2.12-2.18, m, 1H 2.32, dt (14.2, 5.9), 1H	34.3	34.29
5	4.36, m (11.5, 8, 3.5)	4.37, ddd (10.6, 9, 3.4)	68.1	68.11
6	5.10, d (11.5)	5.09, d (9.3)	129.4	129.35
7			135.7	135.76
8	1.88, dd (14.5, 10) 2.64, dd (14.5, 4)	1.89, dd (14.4, 10) 2.64, dd (14.8, 4)	44.6	44.60
9	3.84, tdd (10, 4, 1.5)	3.84, tdd (10.2, 4, 1.8)	68.7	68.70
10	1.93, dd (14, 10.5) 2.67, d (14)	1.94, dd (14.1, 10.5) 2.67, d (14)	43.6	43.61
11			142.5	142.50
12	2.22, m 2.42, dd (16, 3.5)	2.22, m, 1H 2.42, dd (14.3, 3.5)	38.4	38.41

13	5.21, tt (7, 3.5)	5.21, tt (7.5, 4.3)	71.4	71.32
14	2.15, m 2.30, m	2.12-2.18, m, 1H 2.27, m, 1H	39.5	39.46
15			145.1	145.14
16	2.05, t (7), 2H	2.04, t (7.9), 2H	35.6	35.56
19	3.94, pent (6)	3.94, pent (6)	69.1	69.14
21	4.13, sext (6.5)	4.15, sext (6.0)	65.5	65.56
22	1.22, d, (6.5), 3H	1.22, d, (6.3), 3H	23.6	23.65
23	1.77, s, 3H	1.77, d, (1.5), 3H	20.1	20.14
24	4.95, s 5.08, s	4.96, d, (1.9), 1H 5.08, s, 1H	117.9	117.96
25	4.72, s 4.78, s	4.72, s, 1H 4.78, d, (1.7), 1H	112.6	112.62
3	1.59, m, 2H	1.22-1.75, m, 9H	21.5	21.51
17	1.48, m, 2H		23.7	23.67
18	1.46, m, 2H		36.9	36.90
20	1.58, m, 2H		44.2	44.16
4	1.44, m		36.5	36.54
	1.88, m	1.78-1.83, m		

Scheme 4.20 Comparison of the ^{1}H and ^{13}C NMR Spectra of **Isomer2** (**4.55**) and the Natural Product Arenolide



	δ_H		δ_C	
	Natural (400 MHz)	Synthetic (600 MHz)	Natural (100 MHz)	Synthetic (150 MHz)
1			172.5	172.53
2	2.12, m 2.33, m	2.12-2.19, m, 1H 2.30-2.35, m	34.3	34.35
5	4.36, m (11.5, 8, 3.5)	4.37, td (10.4, 3.3))	68.1	68.11
6	5.10, d (11.5)	5.09, d (12.1)	129.4	129.33
7			135.7	135.77
8	1.88, dd (14.5, 10) 2.64, dd (14.5, 4)	1.89, dd (14.4, 10) 2.64, dd (13.5, 4.4)	44.6	44.61
9	3.84, tdd (10, 4, 1.5)	3.84, t (9.1)	68.7	68.71
10	1.93, dd (14, 10.5) 2.67, d (14)	1.94, dd (14.0, 10.5) 2.68, d (14.2)	43.6	43.60
11			142.5	142.51
12	2.22, m 2.42, dd (16, 3.5)	2.22-2.30, m, 1H 2.43, dd (14.3, 3.5)	38.4	38.39
13	5.21, tt (7, 3.5)	5.20, tt (7.7, 3.8)	71.4	71.41
14	2.15, m 2.30, m	2.12-2.19, m, 1H 2.22-2.30, m, 1H	39.5	39.48
15			145.1	145.16
16	2.05, t (7), 2H	1.97-2.12, m, 2H	35.6	35.25

19	3.94, pent (6)	3.96, pent (5.8)	69.1	68.80
21	4.13, sext (6.5)	4.15, sext (6.0)	65.5	65.54
22	1.22, d, (6.5), 3H	1.22, d, (6.5), 3H	23.6	23.62
23	1.77, s, 3H	1.77, d, (1.4), 3H	20.1	20.13
24	4.95, s 5.08, s	4.96, s, 1H 5.09, s, 1H	117.9	117.96
25	4.72, s 4.78, s	4.72, s, 1H 4.79, s 1H	112.6	112.72
3	1.59, m, 2H	1.36-1.75, m, 9H	21.5	21.50
17	1.48, m, 2H		23.7	23.62
18	1.46, m, 2H		36.9	36.84
20	1.58, m, 2H		44.2	44.23
4	1.44, m		36.5	36.58
	1.88, m	1.78-1.83, m		

4.5 Conclusions

In summary, we have accomplished the total synthesis of natural product arenolide, whose structure was further determined based on ^{1}H and ^{13}C NMR Spectra of synthesized ones. This synthesis features a catalytic enantioselective Suzuki coupling between geminal bis(boronic) esters and alkenyl halides, enantioselective diboration at terminal mono-substituted alkenes, followed by regioselective Suzuki coupling reaction, which is another important tool applied to construct the relatively complicated structure arenolide. The convergent synthetic strategy allowed the overall synthesis more efficient and modular, which also made it possible to streamline the synthesis of the two possible isomers. The data of these two isomers were also collected and compared with the natural

product, and the one more resembled to the natural product was determined to be (+) arenolide.

4.6 Experimental Section

4.6.1 General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), or a Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm, THF-d_8: 3.58 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qi = quintet, sx = sextet, sp = septet, m = multiplet, br = broad), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.0 ppm, THF-d_8: 67.57 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution

mass spectrometry (DART+) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA.

Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 – 400 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), phosphomolybdic acid (PMA) in ethanol and ceric ammonium molybdate (CAM) in ethanol.

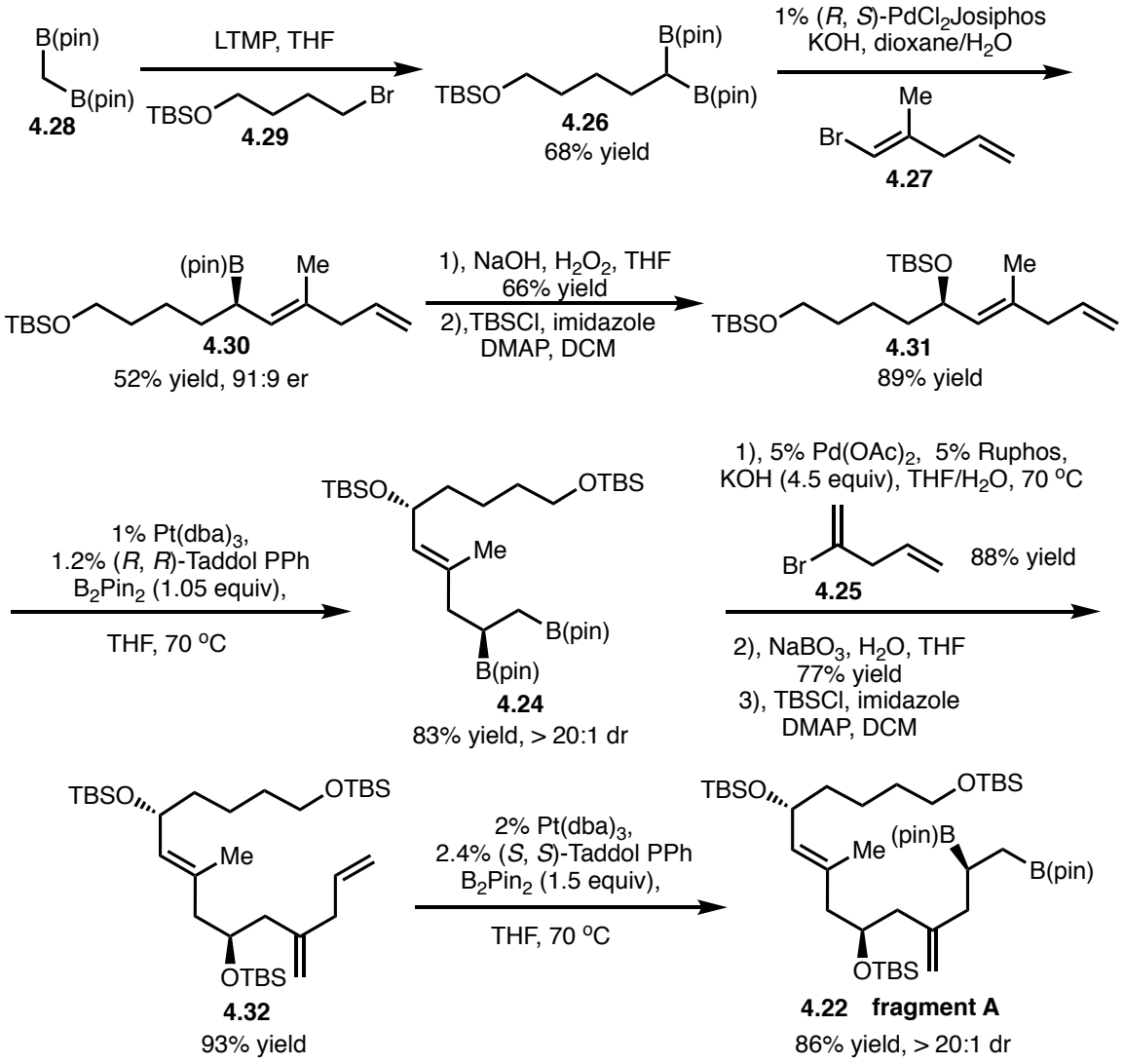
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector.

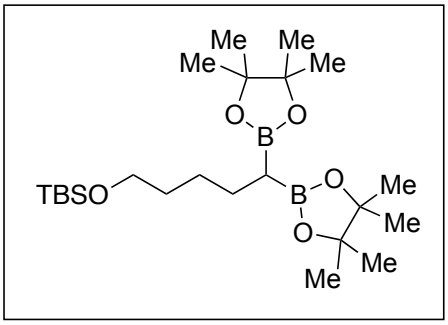
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether, dichloromethane and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon.

Bis(pinacolato)diboron was generously donated by Allychem Co., Ltd. and used without further purification. Triethylamine was purchased from Alfa Aesar and distilled over calcium hydride prior to use. The following reagents were purchased and used without purification: copper(I) iodide (CuI) (Aldrich), lithium 2,2,6,6-tetramethylpiperidide (LTMP) (Aldrich), sodium *tert*-butoxide (NaO*t*-Bu)

(Strem), palmitic acid-1-^{13}C (Cambridge Isotope Laboratories), and *N*,*N*-dimethylformamide (DMF) (Acros). All other reagents were purchased from either Aldrich, Alfa Aesar or Acros and used without further purification.

4.6.2 Full Characterization of Compounds

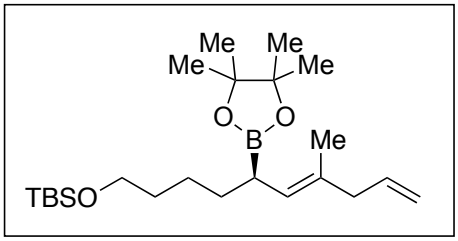




((5,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)oxy)(*tert*-butyl)dimethylsilane (4.26). An oven-dried 50 mL round bottom flask was added 2,2,6,6-tetramethylpiperidine (1.86 mL, 11

mmol) and THF (10 mL). The resulting solution was cooled down to -78 °C. *n*BuLi (4.4 mL, 2.5 M, 11 mmol) was added dropwise into the solution under N_2 protection, which was then warmed to room temperature gradually and stirred for 20 minutes give in orange clear LiTMP (lithium tetramethylpiperidide) solution. Another oven dried 100 mL round bottom flask was added bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane **1** (2.68 g, 10 mmol) and THF (10 mL), The clear colorless solution was cooled to 0 °C. The LiTMP was cooled to 0 °C and added dropwise into the methyl diboronate ester solution, which lead to the formation of an orange cloudy slurry. The slurry was stirred for 10 minutes at 0 °C, and then (4-bromobutoxy)(*tert*-butyl)dimethylsilane (3.47 g, 13 mmol) was added slowly. The mixture was stirred overnight, which resulted in orange cloudy solution. The reaction mixture was then quenched by diethyl ether, filtered through a short pad of silica gel. The filtrate was evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:2 hexanes/ethyl acetate, stain in CAM) to afford **4.26** as a clear colorless oil (3.1 g, 68%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.57 (t, *J* = 6.7 Hz, 2H), 1.57 – 1.53 (m, 2H), 1.50 (p, *J* = 6.9 Hz, 2H), 1.34 – 1.27 (m, 2H), 1.22 (s, 12H), 1.22 (s, 12H), 0.88 (d, *J* = 0.9 Hz, 9H), 0.72 (t, *J* = 7.9 Hz, 1H), 0.03 (d, *J* = 0.8 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 82.86, 63.42, 33.03, 28.83, 25.98, 25.59, 24.82, 24.51, 18.34, -5.26; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.93; IR (neat): 2977.3 (w), 2929.6 (m), 2857.3 (w), 1462.9 (w), 1359.7 (m), 1310.6 (s), 1264.0 (m), 1215.1 (w), 1140.2 (s), 1099.6 (s), 1005.3 (w), 969.4 (m), 835.6 (s), 774.5 (m), 668.2 (w) cm^{-1};

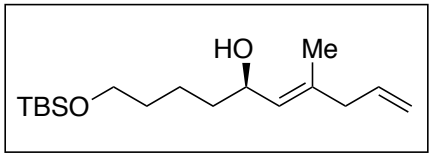
HRMS-(DART+) for $^{12}C_{23}{}^{1}H_{48}{}^{11}B_{2}{}^{16}O_{5}{}^{28}Si_{1}{}^{23}Na_{1}$ $[M+Na]^{+}$: calculated: 477.3355, found: 477.3371.



(*R*,*E*)-*tert*-butyldimethyl((7-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)deca-6,9-dien-1-yl)oxy)silane (4.30). This compound was prepared according to a literature procedure[25] with slightly modification. In the glove box, an oven dried two dram vial was added (*R*)-1-[(*S*)-2-(di*tert*butylphosphanyl)ferrocenyl]ethyldi[4-(trifluoromethyl)phenyl]phosphine with $PdCl_2$ complex (1.8 mg, 0.002 mmol) and 1,4-dioxane (1 mL). The mixture was stirred for five minutes. Then 1,1-diborylalkane (118.1 mg, 0.26 mmol) and (*E*)-1-bromo-2-methylpenta-1,4-diene (32.2 mg, 0.2 mmol) were added. The vial was sealed with a Teflon cap, taken outside of the glove box, and injected with degased 8M KOH (112 μL, 0.9 mmol). The orange clear solution was allowed to stir for 24 hours, resulting in a brown clear solution. This solution was extracted with diethyl ether, filtered through a short pad of silica gel pipet and concentrated *in vacuo*. The crude reaction mixture was then purified on silica gel (hexanes: ethyl acetate = 100:0.4 to 100:2) to afford **4.30** as a colorless oil (45.8 mg, 52%, 78% ee). ^{1}H NMR (600 MHz, $CDCl_3$): δ

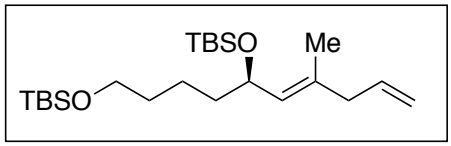
[25] Potter, B.; Szymaniak, A. A.; Edelstein, E. K.; Morken. J. P. *J. Am. Chem. Soc.* **2014**, *136,* 17918-17921.

5.76 (ddt, J = 16.8, 10.0, 6.7 Hz, 1H), 5.08 (dd, J = 9.7, 1.3 Hz, 1H), 5.01 (dq, J = 17.1, 1.7 Hz, 1H), 4.96 (ddt, J = 10.0, 2.3, 1.2 Hz, 1H), 3.58 (t, J = 6.6 Hz, 2H), 2.70 (d, J = 6.8, 1.5 Hz, 2H), 1.95 (dt, J = 9.6, 7.5 Hz, 1H), 1.58 (d, J = 1.3 Hz, 3H), 1.55 – 1.45 (m, 3H), 1.43 – 1.32 (m, 2H), 1.30 – 1.23 (m, 1H), 1.22 (s, 6H),1.21 (s, 6H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 137.52, 132.56, 126.63, 115.15, 82.87, 63.31, 44.30, 33.02, 31.32, 25.99, 25.56, 24.69, 24.54, 18.35, 16.34, -5.26; ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.98; IR (neat): 2977.1 (w), 2953.6 (w), 2928.7 (m), 2856.7 (m), 1471.6 (w), 1370.3 (m), 1317.5 (s), 1254.8 (m), 1214.9 (w), 1143.3 (s), 1099.8 (s), 1005.2 (w), 967.5 (w), 909.7 (w), 835.7 (s), 774.9 (m), 663.2 (w) cm^{-1}; $[\alpha]_D$ +2.2° (*c* 1.14, $CHCl_3$).



(*R*,*E*)-1-((*tert*-butyldimethylsilyl)oxy)-7-methyldeca-6,9-dien-5-ol (S4.1). THF (2 mL) and H_2O (1 mL) were added into a scintillation vial with (*R*,*E*)-*tert*-butyldimethyl((7-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)deca-6,9-dien-1-yl)oxy)silane (45.8 mg, 0.11 mmol). The vial was cooled to 0 °C and charged with sodium perborate monohydrate (109.8 mg, 1.1 mmol). The white cloudy slurry was allowed to stir overnight. The crude reaction mixture was purified by column chromatography on silica gel (100:1 hexanes/ethyl acetate, stain in CAM) to afford **4.1** as a colorless oil (21.7 mg, 66%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.77 (ddt, J = 17.0, 10.1,

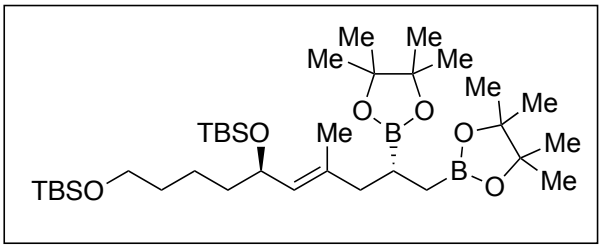
6.9 Hz, 1H), 5.20 (ddt, *J* = 8.7, 2.5, 1.3 Hz, 1H), 5.09 – 5.00 (m, 2H), 4.36 (dt, *J* = 8.5, 6.5 Hz, 1H), 3.60 (t, *J* = 6.5 Hz, 2H), 2.73 (d, *J* = 6.9 Hz, 2H), 1.67 (s, 3H), 1.64 – 1.57 (m, 1H), 1.56 – 1.51 (m, 2H), 1.48 – 1.29 (m, 4H), 0.89 (d, *J* = 0.9 Hz, 9H), 0.04 (d, *J* = 0.9 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 136.95, 136.14, 128.80, 116.28, 68.64, 63.09, 43.92, 37.42, 32.71, 25.96, 21.74, 18.36, 16.62, -5.29; IR (neat): 3333.1 (br, w), 2928.7 (m), 2857.2 (m), 1637.3 (w), 1471.7 (w), 1462.1 (w), 1432.9 (w), 1385.9 (w), 1360.9 (w), 1253.4 (m), 1098.3 (s), 1004.4 (m), 912.3 (m), 833.3 (s), 733.4 (s), 712.6 (w), 661.4 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{17}{}^{1}H_{34}{}^{16}O_2{}^{28}Si_1{}^{23}Na_1$ $[M+Na]^+$: calculated: 321.2226, found: 321.2228; $[\alpha]_D$ +5.9° (*c* 1.09, $CHCl_3$).



(*R*,*E*)-2,2,3,3,11,11,12,12octamethyl-5-(2-methyl penta-1,4-dien-1-yl)-4,10-dioxa-3,11-disilatridec ane (**4.31**).

(*R*,*E*)-1-((*tert*-butyldimethylsilyl)oxy)-7-methyldeca-6,9-dien-5-ol **(S4.1)** (235 mg, 0.79 mmol), DCM (3 mL), and imidazole (133.9 mg, 1.97 mmol) were added into a 20 mL scintillation vial sequentially. The solution was stirred until all solids dissolved, and was then cooled to 0 °C. *tert*-Butyldimethylsilyl chloride (130 mg, 0.87 mmol) was subjected slowly into the above solution. A tip (about 2 mg) of 4-(dimethylamino)pyridine was then added. The white slurry was allowed to stir

overnight, which was then quenched by water, extracted with DCM and filtered through a sodium sulfate padded pipet. The colorless solution was concentrated *in vacuo* to give a colorless oil. The crude reaction mixture was purified by column chromatography on silica gel (100:0.5 – 100:3 hexanes/ethyl acetate, stain in CAM) to afford **5** as a colorless oil (290 mg, 89%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.81 – 5.68 (m, 1H), 5.15 (dt, *J* = 8.7, 1.3 Hz, 1H), 5.08 – 4.94 (m, 2H), 4.31 (td, *J* = 7.7, 5.0 Hz, 1H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.69 (d, *J* = 7.8 Hz, 2H), 1.60 (s, 3H), 1.53 – 1.46 (m, 2H), 1.39 – 1.33 (m, 2H), 1.32 – 1.24 (m, 2H), 0.89 (s, 9H), 0.87 (s, 9H), 0.04 (s, 6H), 0.02 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.46, 132.77, 130.51, 115.94, 69.79, 63.24, 43.99, 38.37, 32.86, 25.99, 25.92, 21.83, 18.57,18.51, 16.51, -4.17, -4.76, -5.28; IR (neat): 2928.6 (m), 2856.7 (m), 1252.24 (s), 1096.2 (s), 1004.5 (m), 938.3 (m), 912.9 (m), 832.0 (s), 771.8 (s), 664.0 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{23}{}^{1}H_{48}{}^{16}O_2{}^{28}Si_2{}^{23}Na_1$ $[M+Na]^+$: calculated: 435.3091, found: 435.3081; $[\alpha]_D$ +1.9° (*c* 1.26, $CHCl_3$).



(*Z*)-2,2'-(6-phenylhex-5-ene-1,1-diyl) bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)) (4.24). The reaction was

performed according to a previous procedure[26] with slightly modification. To an oven dried 2-dram vial were added $Pt(dba)_3$ (8.1 mg, 0.009 mmol), (*R,R*)-3,5-di-iso-propylphenyl-TADDOLPPh (9.8 mg, 0.011 mmol), $B_2(pin)_2$ (240 mg, 0.945 mmol) and THF (0.9 mL) in the glove box. The vial was sealed with Teflon cap and heated at 70 °C for 20 minutes outside of the glovebox. The mixture was cooled to room temperature, and brought back into the glove box again. The solution was charged with

(*R,E*)-2,2,3,3,11,11,12,12-octamethyl-5-(2-methylpenta-1,4-dien-1-yl)-4,10-dioxa-3,11-disilatridecane **4.31** (357mg, 0.9 mmol). The vial was heated at 70 °C outside of the glove box for 12 hours. Upon completion, the yellow solution was extracted with diethyl ether, filtered through a silica gel pipet and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:1 – 100:3 hexanes/ethyl acetate, stain in CAM) to afford **4.24** as a light yellow clear oil (500 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.12 (d, *J* = 8.7 Hz, 1H), 4.29 (td, *J* = 8.0, 5.2 Hz, 1H), 3.58 (t, *J* = 6.6 Hz, 2H), 2.20 (dd, *J* = 13.6, 7.0 Hz, 1H), 1.93 (dd, *J* = 13.6, 8.2 Hz, 1H), 1.57 (s, 3H), 1.53 – 1.44 (m, 3H), 1.39 – 1.32 (m, 1H), 1.32 – 1.24 (m, 3H), 1.22 (s, 24H), 0.89 (s, 9H), 0.86 (s, 9H), 0.77 (dd, *J* = 13.5, 7.5 Hz, 2H), 0.04 (s, 6H), 0.00 (d, *J* = 8.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.06, 130.36, 82.82, 82.74, 69.85, 63.31, 43.14, 38.50,

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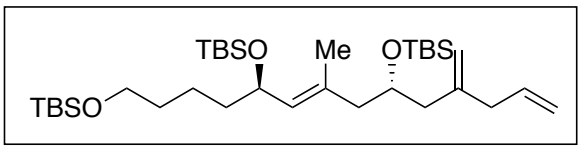
[26] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386-390.

32.90, 25.99, 25.93, 24.91, 24.88, 24.83, 24.76, 21.88, 18.37, 18.22, 16.08, -4.17, -4.82, -5.28; ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.08; IR (neat): 2976.9 (w), 2954.6 (m), 2929.3 (s), 2856.9 (m), 1471.8 (w), 1370.4 (m), 1315.3 (m), 1253.8 (m), 1143.2 (m), 1095.8 (m), 968.9 (w), 834.9 (s), 774.1 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{35}{}^{1}H_{76}{}^{11}B_2{}^{16}O_6{}^{28}Si_2{}^{14}N_1$ $[M+NH_4]^+$: calculated: 684.5397, found: 684.5419; $[\alpha]_D$ +6.9° (*c* 1.35, $CHCl_3$).



(5*R*,9*R*,*E*)-9-((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,7,15,15,16,16-nonamethyl-5-(2-methylenepent-4-en-1-yl)-4,14-dioxa-3,15-disilaheptadec-7-ene (4.32). The reaction was performed according to a previous procedure[27] with slightly modification. In the glove box, an oven dried 20 mL vial was added $Pd(OAc)_2$ (7.52 mg, 0.0335 mmol), Ruphos (15.63 mg, 0.0335 mmol) and THF (6 mL). The mixture was allowed to stir for 5 minutes before adding **4.24** (445 mg, 0.67 mmol), and 2-bromopenta-1,4-diene (394 mg, 2.68 mmol) sequentially. The vial was sealed and brought outside of the glove box. Degassed 8M KOH (0.376 mL, 3.02 mmol) and degassed H_2O (0.6 mL) were added into the vial. The vial was heated at 70 °C overnight. The solution changed color from orange red to black. The reaction mixture

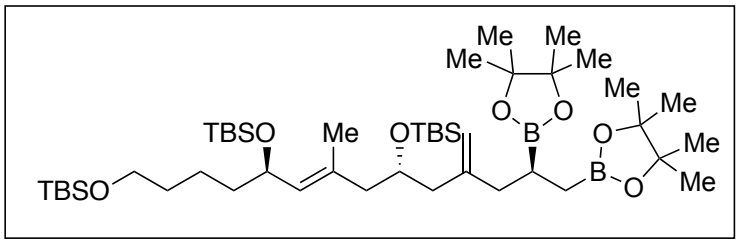
[27] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386-390.

was then extracted with diethyl ether, dried over Na_2SO_4 and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:1 – 100:3 hexanes/ethyl acetate, stain in CAM) to afford **(***R*)-2,2,3,3,11,11,12,12-octamethyl-5-((*R*,*E*)-2-methyl-6-methylene-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)nona-1,8-dien-1-yl)-4,10-dioxa-3,11-disilatridecane **S4.2** as a yellow clear oil (358 mg, 88%).

This compound **S4.2** was oxidized as follows: A 20 mL scintillation vial was added boronic ester **S4.2**, THF (8 mL) and H_2O (8 mL). The solution was cooled to 0 °C, and then subjected with sodium perborate monohydrate (439.9 mg, 4.4 mmol). The mixture was allowed to stir overnight. The solution was quenched by H_2O, extracted with diethyl ether, dried over Na_2SO_4 and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:1 – 100:3 hexanes/ethyl acetate, stain in CAM) to afford (6*R*,10*R*,*E*)-10,14-bis((*tert*-butyldimethylsilyl)oxy)-8-methyl-4-methylenetetradeca-1,8-dien-6-ol **S4.3** as a colorless oil (335 mg, 77%).

The alcohol **S4.3** was protected as shown: alcohol **S4.3** (277 mg, 0.56 mmol), DCM (2 mL) and imidazole (95 mg, 1.4 mmol) were added into a 20 mL scintillation vial sequentially. The mixture was stirred until all solids dissolved, and was then cooled to 0 °C. *tert*-Butyldimethylsilyl chloride (92.4 mg, 0.61 mmol) was added slowly into the above solution. A tip (about 2 mg) of 4-(dimethylamino)pyridine was then added. The

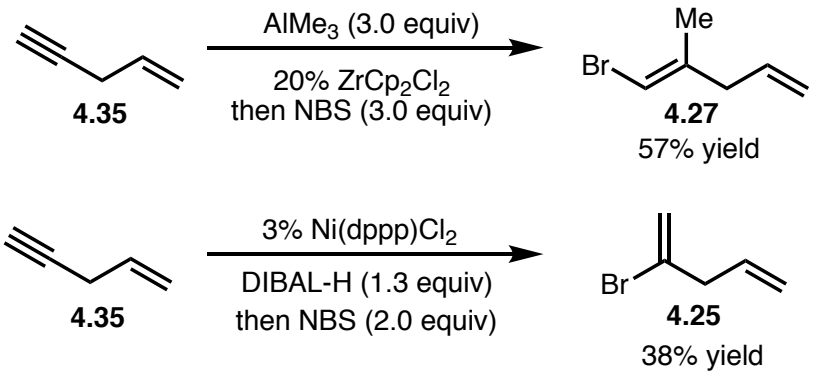
white slurry was allowed to stir overnight, which was then quenched by water, extracted with DCM and dried over Na_2SO_4. The colorless solution was concentrated *in vacuo* to give a colorless oil. The crude reaction mixture was purified by column chromatography on silica gel (100:0 – 100:6 pentane/diethyl ether stain in CAM) to afford **4.32** as a colorless oil (316 mg, 93%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.85 – 5.74 (m, 1H), 5.16 (d, J = 8.7 Hz, 1H), 5.08 – 5.00 (m, 2H), 4.81 (d, J = 11.6 Hz, 2H), 4.31 (td, J = 7.7, 4.8 Hz, 1H), 3.99 – 3.86 (m, 1H), 3.59 (t, J = 6.5 Hz, 2H), 2.76 (d, J = 7.1 Hz, 2H), 2.21 – 2.14 (m, 2H), 2.09 (ddd, J = 16.6, 13.7, 7.0 Hz, 2H), 1.63 (s, 3H), 1.54 – 1.47 (m, 3H), 1.45 – 1.32 (m, 2H), 1.33 – 1.23 (m, 1H), 0.89 (d, J = 0.8 Hz, 9H), 0.87 (d, J = 0.7 Hz, 9H), 0.87 (d, J = 0.8 Hz, 9H), 0.05 – -0.00 (m, 18H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 145.17, 136.34, 132.53, 131.34, 116.19, 113.06, 69.77, 69.63, 63.22, 47.83, 43.62, 41.08, 38.31, 32.86, 25.98, 25.90, 25.88, 21.81, 18.37, 18.20, 18.06, 17.07, -4.21, -4.41, -4.45, -4.75, -5.29; IR (neat): 2928.6 (m), 2856.4 (m), 1471.9 (w), 1361.0 (w), 1252.1 (s), 1089.8 (s), 1004.7 (m), 938.5 (m), 912.5 (m), 831.3 (s), 771.4 (s), 735.4 (m), 663.2 (m) cm^{-1}. HRMS-(DART+) for $^{12}C_{34}{}^{1}H_{71}{}^{16}O_3{}^{28}Si_3$ $[M+H]^+$: calculated: 611.4711, found: 611.4717; $[\alpha]_D$ +7.6° (*c* 0.95, $CHCl_3$).

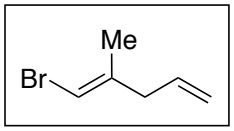


(*E*)-2,2'-(1,8-diphenyloct-7-ene-3,3-diyl)bis(4,4,5,5-tetr

amethyl-1,3,2-dioxaborolane) (4.22). An oven dried 2-dram vial was added $Pt(dba)_3$ (9.3 mg, 0.01 mmol), (*S,S*)-3,5-di-iso-propylphenyl-TADDOLPPh (11.4 mg, 0.013 mmol), $B_2(pin)_2$ (198 mg, 0.78 mmol) and THF (1 mL) in the glove box. The vial was sealed with Teflon cap, taken outside of the glove box and heated at 70 °C for twenty minutes. The vial was cooled to room temperature, and brought back into the glove box again to add **4.32** (316 mg, 0.52 mmol). The vial was then heated at 70 °C outside of the glove box for 12 hours. Upon completion, the yellow solution was extracted with diethyl ether, filtered through a silica gel pipet and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:1 – 100:4 hexanes/ethyl acetate, stain in CAM) to afford **4.22** as a light yellow clear oil (385 mg, 86%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.15 (d, *J* = 8.5 Hz, 1H), 4.78 (d, *J* = 1.9 Hz, 1H), 4.73 (d, *J* = 1.9 Hz, 1H), 4.37 – 4.25 (m, 1H), 3.91 (p, *J* = 6.3 Hz, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 2.23 (dd, *J* = 14.5, 7.2 Hz, 1H), 2.19 – 2.04 (m, 4H), 1.98 (dd, *J* = 14.5, 8.4 Hz, 1H), 1.62 (s, 3H), 1.53 – 1.46 (m, 2H), 1.44 – 1.24 (m, 5H), 1.24 – 1.15 (m, 24H), 0.92 – 0.84 (m, 27H), 0.83 – 0.79 (m, 2H), 0.07 – -0.03 (m, 18H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.38, 132.35, 131.66, 112.50, 82.78, 70.17, 69.69, 63.28, 47.38, 43.77, 40.25, 38.27, 32.87, 31.57, 25.99, 25.96, 25.90, 24.86, 24.84, 24.80, 24.78, 22.64, 21.85, 18.37, 18.20, 18.05, 16.98, 14.09, -4.13, -4.31, -4.48, -4.77, -5.28; ^{11}B NMR (160 MHz, $CDCl_3$) δ 34.76; IR (neat): 2980.1 (w), 2927.0 (w), 1731.8 (s), 1494.7 (w), 1453.7 (w), 1367.9 (m), 1149.3 (m), 1029.9 (m), 968.2 (w), 923.2 (w), 762.1 (w), 700.3 (s) cm^{-}1;

HRMS-(DART+) for $^{12}C_{46}{}^{1}H_{94}{}^{11}B_2{}^{16}O_7{}^{28}Si_3{}^{23}Na_1$ $[M+Na]^+$: calculated: 887.6391, found: 887.6410; $[\alpha]_D$ +6.7° (*c* 0.86, $CHCl_3$).

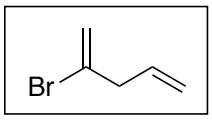




(*E*)-1-bromo-2-methylpenta-1,4-diene (4.27). The reaction was performed according to a previous procedure[28] with slightly modification. An oven dried 100 mL three necked round bottom flask was charged with bis(pentamethylcyclopentadienyl)zirconium dichloride (2.92g, 10 mmol) and DCM (15 mL). The mixture was then allowed to stir for 10 minutes. $AlMe_3$ (3.16 mL, 33 mmol) was added into the flask dropwise at room temperature under nitrogen protection. The mixture was stirred at room temperature for 30 minutes before being cooled to -78 °C. 1-Penten-4-yne (0.9 mL, 10 mmol) was added into the above mixture slowly at -78 °C. The solution was allowed to warm up to room temperature gradually and stirred overnight. The flask was cooled to -78 °C again, and NBS (5.3 g, 30

[28] Zhu, G.; Negishi, E. I. *Chem. - Eur. J.* **2008**, *14*, 311-318.

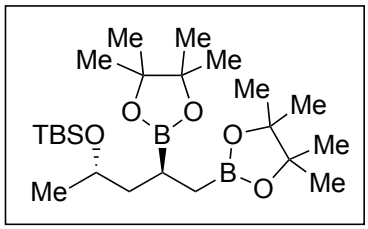
mmol) dissolved in diethyl ether (60 mL) was added as a slurry into the flask under nitrogen protection. The solution was allowed to warm up to room temperature and stirred for another three hours. Upon completion, the reaction mixture was poured into a beaker (containing 2 M HCl (30 mL) and ice chips), the layers were separated and the aqueous layer was extracted with pentane three times. The organic layers were combined, dried over Na_2SO_4 and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (pure pentane, stain in CAM) to afford **4.27** as a clear colorless oil (920 mg, 57%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.95 (s, 1H), 5.75 (ddt, J = 18.6, 9.5, 6.8 Hz, 1H), 5.13 – 4.94 (m, 2H), 2.83 (d, J = 6.8 Hz, 2H), 1.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 140.08, 134.69, 117.14, 102.30, 42.50, 19.16; IR (neat): 2978.9 (m), 2924.1 (s), 2869.2 (s), 2854.7 (s), 1457.1 (w), 1380.6 (w), 1142.2 (s), 419.5 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_6{}^1H_{10}{}^{79}Br$ $[M+H]^+$: calculated: 160.9966, found: 160.9966.



2-bromopenta-1,4-diene (4.25). The reaction was performed according to a previous procedure[29] with slightly modification. An oven dried 100 mL three necked round bottom flask was charged with nickel(II) chloride ($Ni(dppp)Cl_2$, 162.6 mg, 0.3 mmol) in the glove box. Outside of the glove box, THF (10

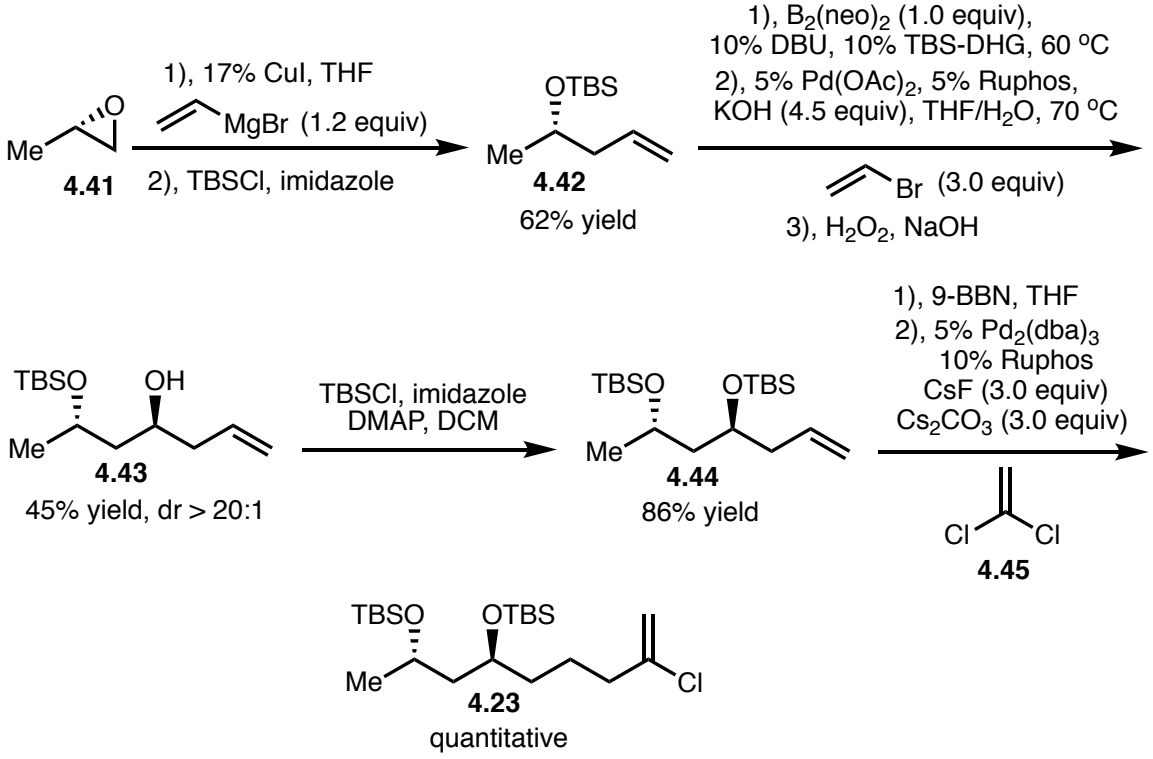
[29] Gao, F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10961-10963.

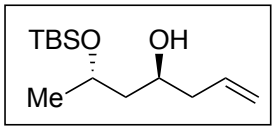
mL) and diisobutylaluminum hydride (neat, 2.32 mL, 13 mmol) were added sequentially into the flask under nitrogen protection. The mixture was stirred for ten minutes at room temperature before being cooled to 0 °C. Then 1-penten-4-yne (0.9 mL, 10 mmol) was added dropwise into the flask. The solution was allowed to warm up to room temperature gradually, and stirred for another two hours to resulting in a black slurry. The flask was cooled to 0 °C again, and subjected with *N*-bromosuccinimide (3.2 g, 18 mmol), which was dissolved in diethyl ether (30 mL). The solution was then warmed up to room temperature gradually, and stirred for another three hours. The reaction mixture was then poured into a separatory funnel containing Rochelle's salt (50 mL) and Et_2O (50 mL). The aqueous layer was then extracted with Et_2O (50 mL) twice. Organic layers were combined, dried over Na_2SO_4, and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (pure pentane, stain in $KMnO_4$) to afford **4.25** as a colorless oil (558 mg, 38%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.88 – 5.79 (m, 1H), 5.62 (d, J = 1.5 Hz, 1H), 5.45 (d, J = 1.6 Hz, 1H), 5.22 – 5.15 (m, 2H), 3.18 (d, J = 6.7 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.78, 131.90, 117.98, 117.15, 45.68; IR (neat): 2955.9 (m), 2930.5 (m), 2870.1 (m), 1716.1 (w), 1630.7 (w), 1435.3 (w), 1379.2 (w), 1363.3 (w), 1251.1 (w) , 1141.8 (s), 1076.4 (m), 918.4 (w), 852.1 (w), 647.0 (w) cm^{-1}.



(((2*S*,4*S*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-yl)oxy)(*tert*-butyl)dimethylsilane (**S4.4**). To an oven dried 2-dram vial was added $Pt(dba)_3$ (2.7 mg, 0.003 mmol), (*S*,*S*)-3,5-di-iso-propylphenyl-TADDOLPPh (2.9 mg, 0.0036 mmol), $B_2(pin)_2$ (80 mg, 0.315 mmol) and THF (0.3 mL) in the glove box. The vial was sealed with Teflon cap, taken outside of the glove box, and heated at 70 °C for twenty minutes. The mixture was cooled to room temperature, and returned to the glove box again to add (*S*)-*tert*-butyldimethyl(pent-4-en-2-yloxy)silane **4.42** (60 mg, 0.3 mmol). The vial was then heated at 70 °C outside of the glove box for 12 hours. Upon completion, the yellow solution was extracted with diethyl ether, filtered through a silica gel pipet and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:3 to 100:5 hexanes/ethyl acetate, stain in CAM) to afford **S3** as a colorless oil (130 mg, 95%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.85 (h, *J* = 6.2 Hz, 1H), 1.54 (dt, *J* = 13.9, 7.1 Hz, 1H), 1.42 (dt, *J* = 13.6, 7.0 Hz, 1H), 1.22 (s, 24H), 1.26 – 1.16 (m, overlap, 1H), 1.10 (d, *J* = 6.1 Hz, 3H), 0.88 (s, 9H), 0.83 (d, *J* = 7.5 Hz, 2H), 0.04 (d, *J* = 4.5 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 82.82, 82.71, 68.25, 43.30, 25.98, 24.87, 24.81, 24.74, 23.74, 18.15, -4.38, -4.61; IR (neat): 2976.6 (m), 2928.6 (w), 2856.7 (w), 1437.9 (w), 1369.8 (s), 1313.2 (s), 1252.8 (m), 1213.8 (w), 1139.9 (s), 1068.8 (m), 1003.2 (m), 968.6 (m), 834.1 (s), 808.1 (m), 773.4 (s), 671.8 (w) cm^{-1};

HRMS-(DART+) for $^{12}C_{23}{}^{1}H_{48}{}^{11}B_{2}{}^{16}O_{5}{}^{28}Si_{1}{}^{23}Na_{1}$ $[M+Na]^{+}$: calculated: 477.3355, found: 477.3374; $[\alpha]_D$ +0.2° (*c* 1.12, $CHCl_3$).





(4*S*,6*S*)-6-((*tert*-butyldimethylsilyl)oxy)hept-1-en-4-ol (**4.43**). The reaction was performed according to a previous procedure[30] with slightly modification. In the glovebox, to an oven-dried 50 mL round bottom flask was added with pseudoenantiomeric glycols 6-tert-butyldimethylsilyl-1,2-dihydroglucal (TBS-DHG) catalyst (79 mg, 0.3 mmol), bis(neopentylglycolato)diboron (677 mg, 3.0

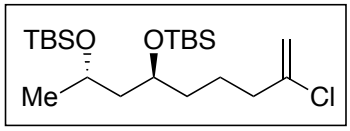
[30] Fang, L.; Yan, L.; Haeffner, F.; Morken, J. P. *J. Am. Chem. Soc.* **2016**, *138*, 2508-2511.

mmol), (*S*)-*tert*-butyldimethyl(pent-4-en-2-yloxy)silane (800 mg, 3.0 mmol, prepared according to literature[31]) and THF (3.0 mL). The mixture was allowed to stir for five minutes before adding DBU (0.045 mL, 0.3 mmol). The vial was then sealed with rubber septum, and removed from the glove box. The mixture was stirred at 60 °C for 24 hours. The flask was cooled to room temperature, returned to the glove box, and charged with $Pd(OAc)_2$ (7.52 mg, 0.0335 mmol) and Ruphos (15.63 mg, 0.0335 mmol). The vial was then taken outside of the glove box. THF (15 mL), 1M vinyl bromide in THF (9 mL, 9.0 mmol) and 8M KOH (1.69 mL, 13.5 mmol) were added sequentially into the flask. The reaction mixture was heated at 70 °C for 12 hours. Upon completion, the flask was cooled to room temperature, subjected with 3 M NaOH (4 mL), and 33% wt H_2O_2 dropwise at 0 °C. After three hours, the flask was cooled to 0 °C, $Na_2S_2O_3$ (aq, 4 mL) was added carefully to quench the reaction. The layers were separated, and the aqueous layer was extracted with diethyl ether twice. The combined organic layers were dried over Na_2SO_4 and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:1-100:10 pentane/diethyl ether, stain in $KMnO_4$) to afford **4.43** as a yellow clear oil (330 mg, 45%, > 20:1 dr). The spectra were in accordance with a previous report.[32] ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 (ddt, J = 17.3, 10.3, 7.1 Hz, 1H), 5.17 – 5.04 (m, 2H), 4.21 (pd, J = 6.1, 3.8 Hz, 1H), 4.05 – 3.96 (m,

[31] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386-390.

[32] Amans, D.; Bellosta, V.; Cossy, J. *Org. Lett.* **2007**, *9*, 1453-1456.

1H), 3.30 (d, *J* = 2.3 Hz, 1H), 2.33 – 2.11 (m, 2H), 1.63 (ddd, *J* = 13.9, 9.9, 3.7 Hz, 1H), 1.53 (ddd, *J* = 14.3, 5.5, 2.3 Hz, 1H), 1.22 (d, *J* = 6.3 Hz, 3H), 0.90 (s, 9H), 0.09 (d, *J* = 4.3 Hz, 6H).



(5*S*,7*S*)-5-(4-chloropent-4-en-1-yl)-2,2,3,3,7,9,9,10,10-nonamethyl-4,8-dioxa-3,9-disilaundecane (**4.44**). (4*S*,6*S*)-6-((*tert*-Butyldimethylsilyl)oxy)hept-1-en-4-ol (**4.43**) (900 mg, 3.68 mmol), DCM (12 mL) and imidazole (626 mg, 9.2 mmol) were added into a 50 mL round bottom flask sequentially. The mixture was stirred until all solids dissolved, and was then cooled to 0 °C. *tert*-Butyldimethylsilyl chloride (610 mg, 4.05 mmol) was subjected slowly into the above solution. Lastly, a tip (about 2 mg) of 4-(dimethylamino)pyridine was added. The white slurry was allowed to stir overnight, which was then quenched by water, extracted with DCM, and dried over Na_2SO_4. The colorless solution was concentrated *in vacuo* to give a colorless oil. The crude reaction mixture was purified by column chromatography on silica gel (100:1-100:2 pentane/diethyl ether, stain in CAM) to afford (5*S*,7*S*)-5-allyl-2,2,3,3,7,9,9,10,10-nonamethyl-4,8-dioxa-3,9-disilaundecane **4.44** as a colorless oil (1.14 g, 86%).

This compound (**4.23**) was prepared according to a previous procedure with slightly modification.[33] In the glove box, to a four dram vial was added 9-BBN dimer (122.0 mg, 0.5 mmol), THF (2 mL) and (5*S*,7*S*)-5-allyl-2,2,3,3,7,9,9,10,10-nonamethyl-4,8-dioxa-3,9-disilaundecane **4.44** (358.7 mg, 1.0 mmol). The mixture was allowed to stir for 1.5 hours to result in yellow clear solution. $Pd_2(dba)_3$ (45.8 mg, 0.05 mmol), Ruphos (46.6 mg, 0.1 mmol), THF (6 mL), CsF (455.7 mg, 3.0 mmol), and Cs_2CO_3 (977.5 mg, 3.0 mmol) were then added sequentially into the vial. The vial was then sealed with a Teflon cap, and taken outside of the glove box. 1,1-Dichloroethylene (0.32 mL, 4.0 mmol) was added into the reaction solution. The vial was then heated at 70 °C for 12 hours. Upon completion, the reaction mixture was diluted with diethyl ether, filtered through a silica gel pipet, and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:0-100:3 pentane/diethyl ether, stain in CAM) to afford **4.23** as a yellow clear oil (421 mg, quantitative). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.14 (d, *J* = 1.0 Hz, 1H), 5.11 (dt, *J* = 1.0 Hz, 1H), 3.88 (h, *J* = 6.4 Hz, 1H), 3.76 (p, *J* = 5.8 Hz, 1H), 2.32 (t, *J* = 7.4 Hz, 2H), 1.65 – 1.57 (m, 3H), 1.54 – 1.39 (m, 3H), 1.14 (d, *J* = 6.2 Hz, 3H), 0.88 (s, 18H), 0.09 – 0.01 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 142.89, 111.89, 69.76, 66.34, 47.87, 39.19, 36.61, 25.91, 24.52, 22.63, 18.08, -3.88, -4.11, -4.23, -4.48; IR (neat): 2953.8 (m),

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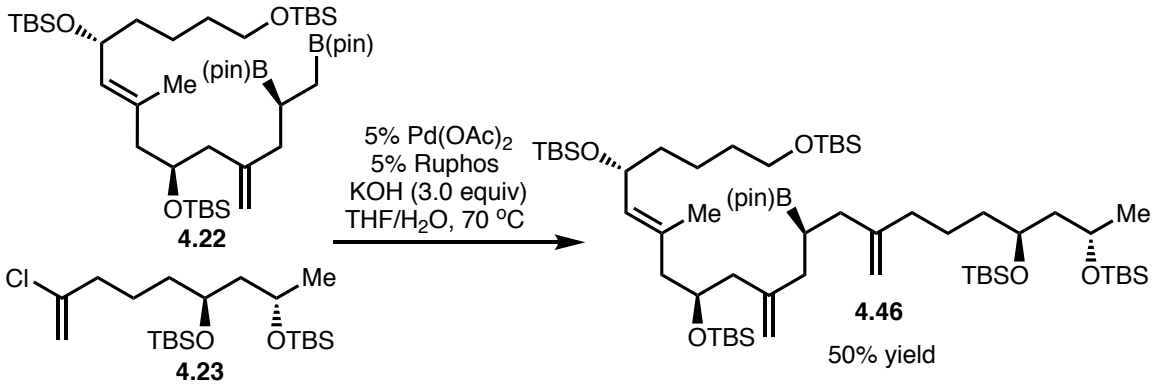
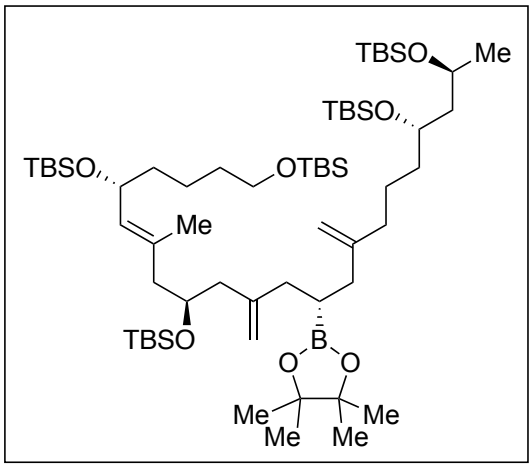
[33] Liron, F.; Fosse, C.; Pernolet, A.; Roulland, E. *J. Org. Chem.*, **2007**, *72*, 2220-2223.

2928.8 (m), 2885.8 (w), 2856.6 (m), 1471.9 (w), 1374.9 (w), 1253.3 (m), 1118.7 (m), 1062.2 (m), 1004.8 (m), 938.9 (w), 872.2 (m), 832.6 (s), 805.6 (m), 771.1 (s), 704.8 (w), 663.9 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{21}{}^{1}H_{45}{}^{35}Cl_{1}{}^{16}O_{2}{}^{28}Si_{2}{}^{23}Na_{1}$ $[M+Na]^{+}$: calculated: 443.2544, found: 443.2545; $[\alpha]_D$ +6.9° (*c* 1.43, $CHCl_3$).



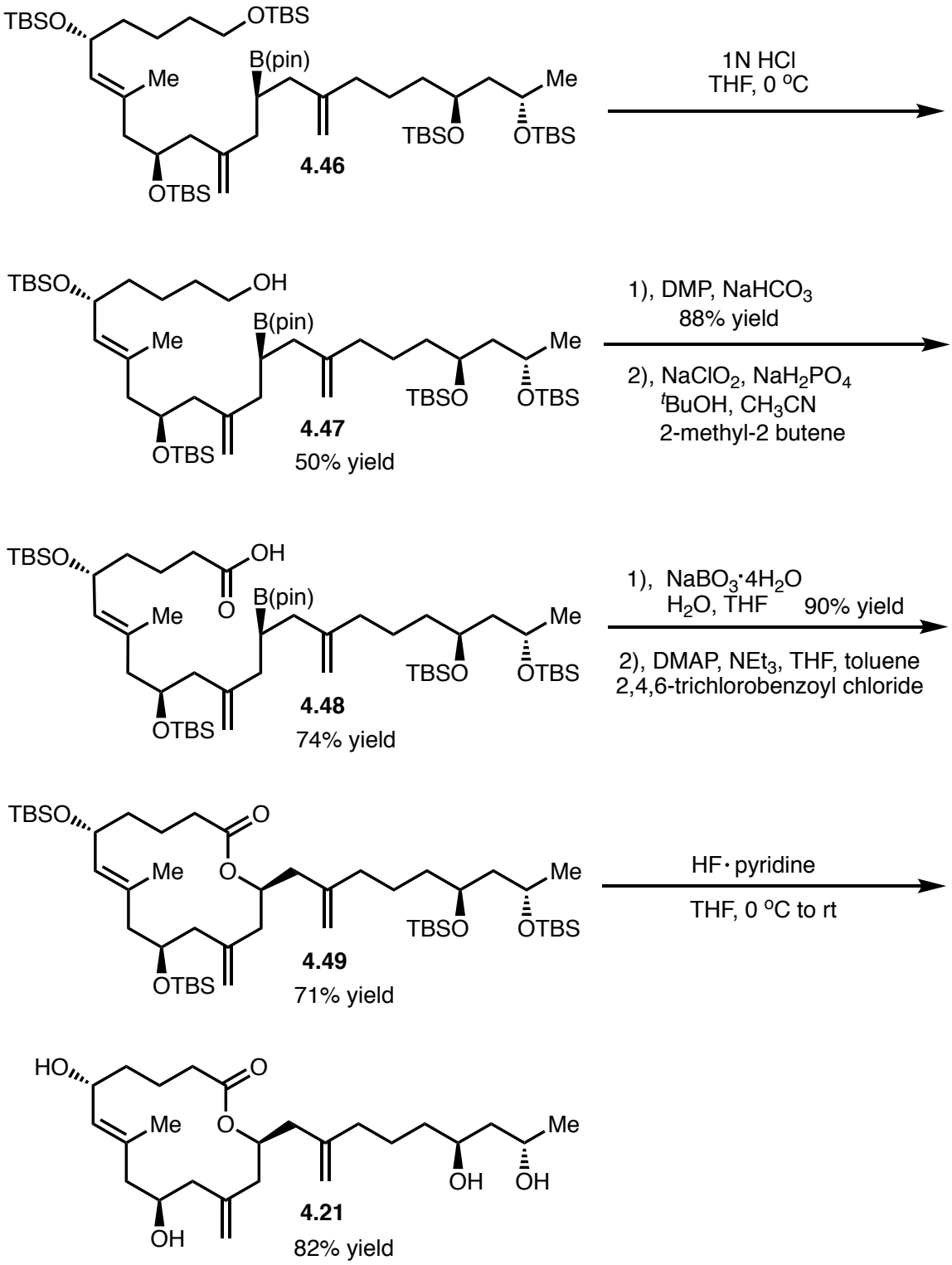


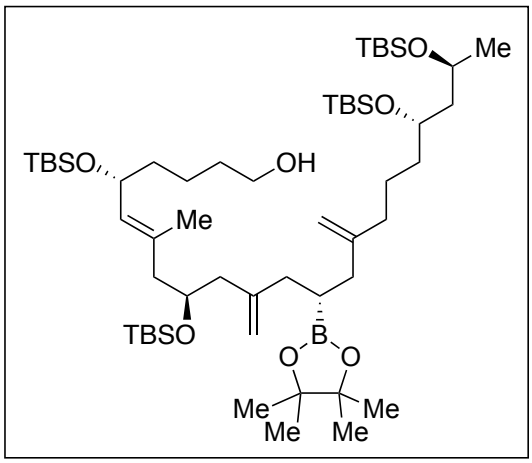
(9*R*,13*R*,17*S*,23*S*,25*S*,*E*)-9,13,23-tris((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,11,25,27,27,28,28-decamethyl-15,19-dimethylene-17-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,26-dioxa-3,27-disilanonacos-10-ene. **(4.16)** The reaction was performed according to a

previous procedure[34] with slightly modification. In the glove box, an oven dried 20 mL vial was added $Pd(OAc)_2$ (7.52 mg, 0.0335 mmol), Ruphos (15.63 mg, 0.0335 mmol) and THF (3 mL). The mixture was allowed to stir for 5 minutes before adding (*E*)-2,2'-(1,8-diphenyloct-7-ene-3,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **4.22** (290 mg, 0.335 mmol) and **4.23** (141.2 mg, 0.335 mmol) sequentially. The vial was sealed and brought outside of the glove box. Degased 8M KOH (0.19 mL, 1.5 mmol) and degassed H_2O (0.3 mL) were added into the vial. The vial was heated at 70 °C overnight. The solution changed color from orange red to black. The reaction mixture was extracted with diethyl ether, dried over Na_2SO_4 and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:0.5-100:1 hexanes/ethyl acetate, stain in CAM) to afford **4.16** as a colorless oil (219 mg, 66%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.16 (d, *J* = 8.5 Hz, 1H), 4.84 (d, *J* = 1.9 Hz, 1H), 4.75 (s, 1H), 4.74 (s, 1H), 4.69 (s, 1H), 4.30 (td, *J* = 8.1, 4.7 Hz, 1H), 3.96 – 3.84 (m, 2H), 3.77 – 3.71 (m, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 2.17 – 2.01 (m, 8H), 1.97 (d, *J* = 7.6 Hz, 2H), 1.67 – 1.56 (m, overlap, 1H), 1.61 (d, *J* = 1.3 Hz, 3H), 1.53 – 1.45 (m, 6H), 1.45 – 1.33 (m, 6H), 1.18 (s, 12H), 1.14 (d, *J* = 6.0 Hz, 3H), 0.91 – 0.82 (m, 45H), 0.08 – -0.04 (m, 30H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 149.09, 146.49, 132.46, 131.46, 112.15, 109.38, 82.89, 70.22, 70.03, 69.66, 66.34, 63.27, 48.00, 47.49, 43.98, 38.46, 38.27, 37.82, 37.57, 36.12,

[34] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386-390.

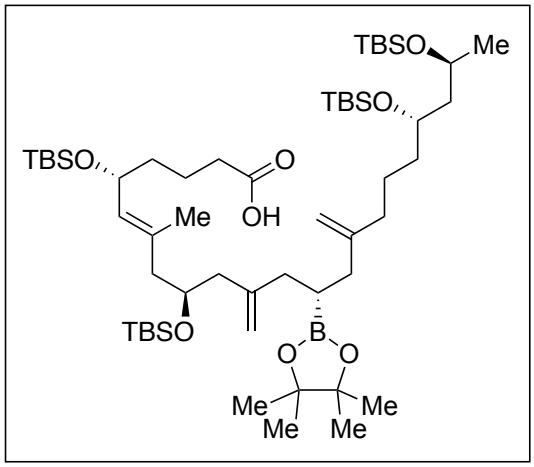
32.87, 25.99, 25.95, 25.93, 25.90, 24.87, 24.81, 24.51, 23.14, 21.86, 19.90 (broad, C-B bond), 18.38, 18.20, 18.10, 18.06, 16.94, -3.88, -4.02, -4.14, -4.21, -4.36, -4.46, -4.75, -5.27; IR (neat): 2953.2 (m), 2928.5 (m), 2886.1 (w), 2856.6 (m), 1471.9 (w), 1380.2 (w), 1253.1 (m), 1143.7 (m), 1091.4 (m), 1065.7 (m), 1005.2 (w), 833.7 (s), 807.4 (m), 772.9 (s), 664.7 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{61}{}^{1}H_{131}{}^{11}B_{1}{}^{16}O_{7}{}^{14}N_{1}{}^{28}Si_{5}$ $[M+NH_4]^+$: calculated: 1140.8865, found: 1140.8893; $[\alpha]_D$ +4.5° (*c* 0.33, $CHCl_3$).


TBSO
OTBS
B(pin)
Me
Me
TBSO
OTBS
OTBS
4.46
1N HCl
THF, 0 °C
TBSO
OH
B(pin)
Me
Me
TBSO
OTBS
OTBS
4.47
50% yield
1), DMP, NaHCO3
88% yield
2), NaClO2, NaH2PO4
tBuOH, CH3CN
2-methyl-2 butene
TBSO
OH
O
B(pin)
Me
Me
TBSO
OTBS
OTBS
4.48
74% yield
1), NaBO3·4H2O
H2O, THF
90% yield
2), DMAP, NEt3, THF, toluene
2,4,6-trichlorobenzoyl chloride
TBSO
O
Me
O
Me
TBSO
OTBS
OTBS
4.49
71% yield
HF·pyridine
THF, 0 °C to rt
HO
O
Me
O
Me
OH
OH
OH
4.21
82% yield



(5*R*,9*R*,13*S*,19*S*,21*S*,*E*)-5,9,19,21-tetrakis((*tert*-butyldimethylsilyl)oxy)-7-methyl-11,15-dimethylene-13-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)docos-6-en-1-ol (**4.47**). To a 20 mL scintillation vial was added **4.46** (80 mg, 0.08 mmol) and THF (8 mL). The solution was cooled to 0 °C and stirred for 15 minutes. HCl (0.08 mL, 1 M, 0.08 mmol) was added dropwise into the mixture, and the solution was stirred at 4 °C (cold room) overnight. The solution was cooled to 0 °C, $Na_2S_2O_3$ (0.5 mL) was added to quench the reaction. The mixture was extracted with diethyl ether, filtered through a pipet of $Na_2S_2O_4$, and evaporated *in vacuo*. The crude reaction mixture was then purified by column chromatography on silica gel (100:1-85:15 hexanes/ethyl acetate, stain in CAM) to afford **4.47** as a clear colorless oil (35 mg, 50%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.16 (d, *J* = 8.4 Hz, 1H), 4.84 (d, *J* = 1.8 Hz, 1H), 4.75 (s, 1H), 4.74 (s, 1H), 4.70 (d, *J* = 1.8 Hz, 1H), 4.33 (td, *J* = 7.6, 4.4 Hz, 1H), 3.94 – 3.86 (m, 2H), 3.78 – 3.70 (m, 1H), 3.63 (t, *J* = 6.7 Hz, 2H), 2.16 – 2.01 (m, 8H), 2.01 – 1.94 (m, 2H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.60 –1.22 (m, 13H), 1.19 (s, 12H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.92 – 0.80 (m, 36H), 0.10 – -0.03 (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.09, 146.45, 132.21, 131.77, 112.21, 109.40, 82.93, 70.24, 70.04, 69.52, 66.35, 62.97, 47.99, 47.45, 43.90, 38.46, 38.18, 37.81,

37.57, 36.14, 32.79, 29.70, 25.95, 25.90, 24.87, 24.80, 24.52, 23.14, 21.59, 19.89 (broad, C-B bond), 18.20, 18.10, 17.09, -3.87, -4.01, -4.13, -4.20, -4.37, -4.45, -4.74; IR (neat): 2953.3 (m), 2928.7 (s), 2884.4 (m), 2856.7 (s), 1472.0 (w), 1462.1 (w), 1380.2 (m), 1253.5 (m), 1143.3 (s), 1086.8 (m), 1067.3 (m), 1005.2 (w), 891.3 (w), 834.7 (s), 807.1 (m), 773.5 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{55}{}^{1}H_{117}{}^{11}B_{1}{}^{16}O_{7}{}^{14}N_{1}{}^{28}Si_{4}$ $[M+NH_4]^+$: calculated: 1026.8000, found: 1026.7988; $[\alpha]_D$ +3.6° (*c* 0.23, $CHCl_3$).



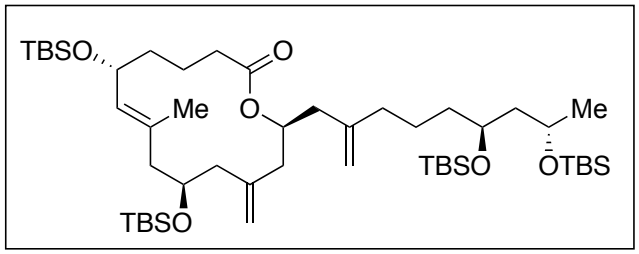
(5*R*,9*R*,13*S*,19*S*,21*S*,*E*)-5,9,19,21-tetrakis((*tert*-butyldimethylsilyl)oxy)-7-methyl-11,15-dimethylene-13-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)docos-6-enoic acid (**4.48**). To a 20 mL scintillation vial was added alcohol **4.47** (35 mg, 0.04 mmol) and DCM (1 mL). The mixture was cooled to 0°C, Dess-Martin periodinane (20 mg, 0.048 mmol) and $NaHCO_3$ (16.6 mg, 0.198 mmol) were added. After 4 hours, the reaction mixture was concentrated *in vacuo*, then extracted by 1:1 hexane/Et_2O, filtered through silica gel padded sintered funnel, rinsed with 1:1 hexane/Et_2O and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:2-100:3 hexanes/ethyl acetate, stain in CAM) to afford (5*R*,9*R*,13*S*,19*S*,21*S*,*E*)-5,9,19,21-tetrakis((*tert*-butyldimethylsilyl)oxy)-7-methyl-11,15-d

imethylene-13-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)docos-6-enal **S4.5** as a clear colorless oil (31 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.75 (t, *J* = 1.9 Hz, 1H), 5.16 (d, *J* = 8.4 Hz, 1H), 4.84 (s, 1H), 4.74 (s, 1H), 4.74 (s, 1H), 4.70 (s, 1H), 4.34 (td, *J* = 7.8, 5.0 Hz, 1H), 3.96 – 3.83 (m, 2H), 3.74 (p, *J* = 4.7 Hz, 1H), 2.41 (td, *J* = 7.5, 2.0 Hz, 2H), 2.17 – 1.95 (m, 10 H), 1.76 – 1.68 (m, 1H), 1.62 (s, 3H), 1.58– 1.23 (m, 10 H), 1.18 (s, 12H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.91 – 0.83 (m, 36H), 0.10 – -0.03 (m, 24H).

(5*R*,9*R*,13*S*,19*S*,21*S*,*E*)-5,9,19,21-Tetrakis((*tert*-butyldimethylsilyl)oxy)-7-methyl -11,15-dimethylene-13-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)docos-6-enoic acid **4.48** was prepared according to a previous procedure[35] with slightly modification. A 20 mL scintillation vial was added aldehyde **S4.5** (4 mg, 0.0045 mmol), ^{t}BuOH (0.438 mL) and 2- methyl-2-butene (0.05 mL, 0.046 mmol) sequentially. The mixture was cooled to 0°C. A solution of $NaClO_2$ (4.92 mg, 0.055 mmol) and NaH_2PO_4 (5.99 mg, 0.046 mmol) in H_2O (0.14 mL) was added into the vial. THF (0.4 mL) was added last. The solution was then allowed to warm up to room temperature and stirred for another hour. The reaction mixture was quenched by H_2O, extracted with diethyl ether, filtered through a $Na_2S_2O_4$ pipet and evaporated *in vacuo*. The crude reaction mixture was then purified by column chromatography on silica gel (100:8-100:20 hexanes/ethyl acetate, stain in CAM) to afford **4.48** as a clear colorless oil (3 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.14 (d,

[35] Paterson, I.; Paquet, T. *Org. Lett.* **2010**, *12*, 2158-2161.

J = 8.7 Hz, 1H), 4.84 (s, 1H), 4.75 (s, 1H), 4.74 (s, 1H), 4.70 (s, 1H), 4.41 – 4.32 (m, 1H), 4.00 – 3.84 (m, 2H), 3.78 – 3.71 (m, 1H), 2.38 – 2.31 (m, 2H), 2.25 – 1.94 (m, 10H), 1.65 (d, *J* = 1.4 Hz, 3H), 1.63 –1.24 (m, 11H), 1.20 (s, 12H), 1.14 (d, *J* = 6.2 Hz, 3H), 0.91 – 0.84 (m, 36H), 0.14 – -0.01 (m, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 174.83, 149.07, 146.35, 132.32, 131.70, 112.44, 109.43, 83.17, 70.29, 70.10, 69.20, 66.40, 47.95, 43.52, 37.78, 37.70, 37.57, 36.17, 33.71, 33.50, 31.93, 29.70, 29.36, 25.94, 25.88, 24.82, 24.76, 24.53, 23.12, 22.70, 20.97, 18.17, 18.12, 18.07, 17.36, 14.12, -3.87, -4.00, -4.15, -4.20, -4.41, -4.44, -4.78.; IR (neat): 2954.6 (s), 2926.0 (s), 2855.3 (s), 1714.2 (w), 1557.1 (w), 1462.4 (m), 1380.3 (m), 1361.1 (m), 1254.1 (m), 1142.4 (s), 1086.5 (m), 835.6 (m), 807.1 (w), 774.4 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{55}{}^{1}H_{115}{}^{11}B_{1}{}^{16}O_{8}{}^{14}N_{1}{}^{28}Si_{4}$ $[M+NH_4]^+$: calculated: 1040.7793, found: 1040.7843. $[\alpha]_D$ -3.6° (*c* 0.4, $CHCl_3$).



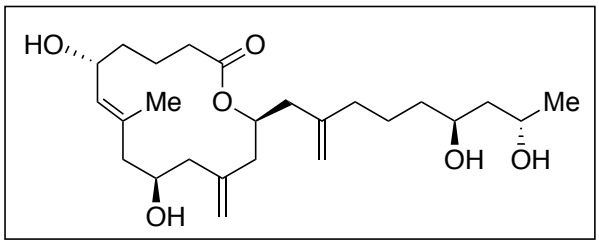
(6*R*,10*R*,14*S*,*E*)-14-((6*S*,8*S*)-6,8-bis((*tert*-butyldimethylsilyl)oxy)-2-methylenenonyl)-6,10-bis((*tert*-butyldimethylsilyl)oxy)-8-methyl-12-methyleneoxacyclotetradec-7-en-2-one (**4.49**). To a 20 mL scintillation vial was added (**4.48**) (6 mg, 0.0067 mmol), THF (1 mL) and H_2O (1 mL). The solution was cooled to 0°C, and sodium perborate monohydrate (30 mg, 0.2 mmol) was added. The mixture was allowed to stir overnight. The solution was quenched by H_2O, extracted with diethyl ether, dried

over Na_2SO_4 and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:0 – 100:20 hexanes/ethyl acetate, stain in CAM) to afford (5*R*,9*R*,13*S*,19*S*,21*S*,*E*)-5,9,19,21-tetrakis((*tert*-butyldimethylsilyl)oxy)-13-hydroxy-7-methyl-11,15-dimethylenedocos-6-enoic acid **S4.6** as a colorless oil (5.5 mg, 90 %).

The Yamaguchi esterification was performed according to a previous procedure.[36] An oven dried 20 mL scintillation vial (charged with a stirring bar, cooled under vacumn) was charged with carboxylic acid **S4.6** (5.5 mg, 6 μmol), THF (1 mL), triethyl amine (6.1 mg, 8.36 μmol) and 2,4,6-trichlorobenzoylchloride (8.8 mg, 72 μmol). The solution was allowed to stir at room temperature for two hours before toluene (4 mL) was added. Then above mixture was then transferred into a syringe. The solution was added into an oven dried 50 mL round bottom flask (precharged with DMAP (8.8 mg, 72 μmol) and toluene (12 mL)) *via* syringe pump at 80 °C over three hours. The mixture was heated at 80 °C overnight, then cooled to room temperature and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:0-100:2 pentane/diethyl ether, stain in CAM) to afford **4.49** as a clear colorless oil (3.8 mg, 71%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.23 – 5.17 (m, 1H), 5.05 (d, *J* = 8.9 Hz, 1H), 4.98 (s, 1H), 4.83 (d, *J* = 2.1 Hz, 1H), 4.76 (d, *J* = 1.8 Hz, 1H), 4.72 (s, 1H), 4.29 (ddd, *J* = 10.3, 8.7,

[36] Williams, D. R.; Patnaik, S.; Plummer, S. V. *Org. Lett.* **2003**, *5*, 5035-5038.

3.2 Hz, 1H), 3.91 – 3.84 (m, 2H), 3.74 (p, *J* = 5.4 Hz, 1H), 2.45 (td, *J* = 14.2, 3.1 Hz, 2H), 2.40 – 2.28 (m, 2H), 2.22 (dd, *J* = 14.3, 6.0 Hz, 2H), 2.18 – 2.08 (m, 2H), 2.01 (td, *J* = 9.9, 3.8 Hz, 3H), 1.92 (dd, *J* = 14.0, 8.9 Hz, 1H), 1.72 (d, *J* = 1.3 Hz, 3H), 1.60 (ddd, *J* = 13.6, 7.1, 5.4 Hz, 2H), 1.54 – 1.46 (m, 1H), 1.46 – 1.39 (m, 5H), 1.33 – 1.24 (m, 2H), 1.13 (d, *J* = 6.2 Hz, 3H), 0.91 – 0.83 (m, 36H), 0.09 – -0.02 (m, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.34, 145.69, 141.95, 132.97, 130.73, 128.00, 117.54, 112.03, 71.69, 71.17, 69.96, 69.24, 66.36, 47.96, 46.66, 43.47, 39.68, 39.15, 38.16, 37.39, 35.91, 34.83, 25.94, 25.93, 25.87, 24.50, 23.01, 21.30, 20.11, 18.20, 18.14, 18.10, -3.89, -4.06, -4.20, -4.36, -4.39, -4.46, -4.66, -4.76; IR (neat): 2954.0 (m), 2928.7 (s), 2856.4 (m), 1735.7 (m), 1472.1 (w), 1462.0 (w), 1374.2 (w), 1361.2 (w), 1253.6 (s), 1144.5 (w), 1117.0 (w), 1087.9 (m), 1050.5 (m), 1005.5 (w), 895.1 (w), 834.9 (s), 807.9 (w), 773.6 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{49}{}^{1}H_{102}{}^{16}O_6{}^{14}N_1{}^{28}Si_4$ $[M+NH_4]^+$: calculated: 912.6784, found: 912.6762; $[\alpha]_D$ +10.1° (*c* 1.03, $CHCl_3$).

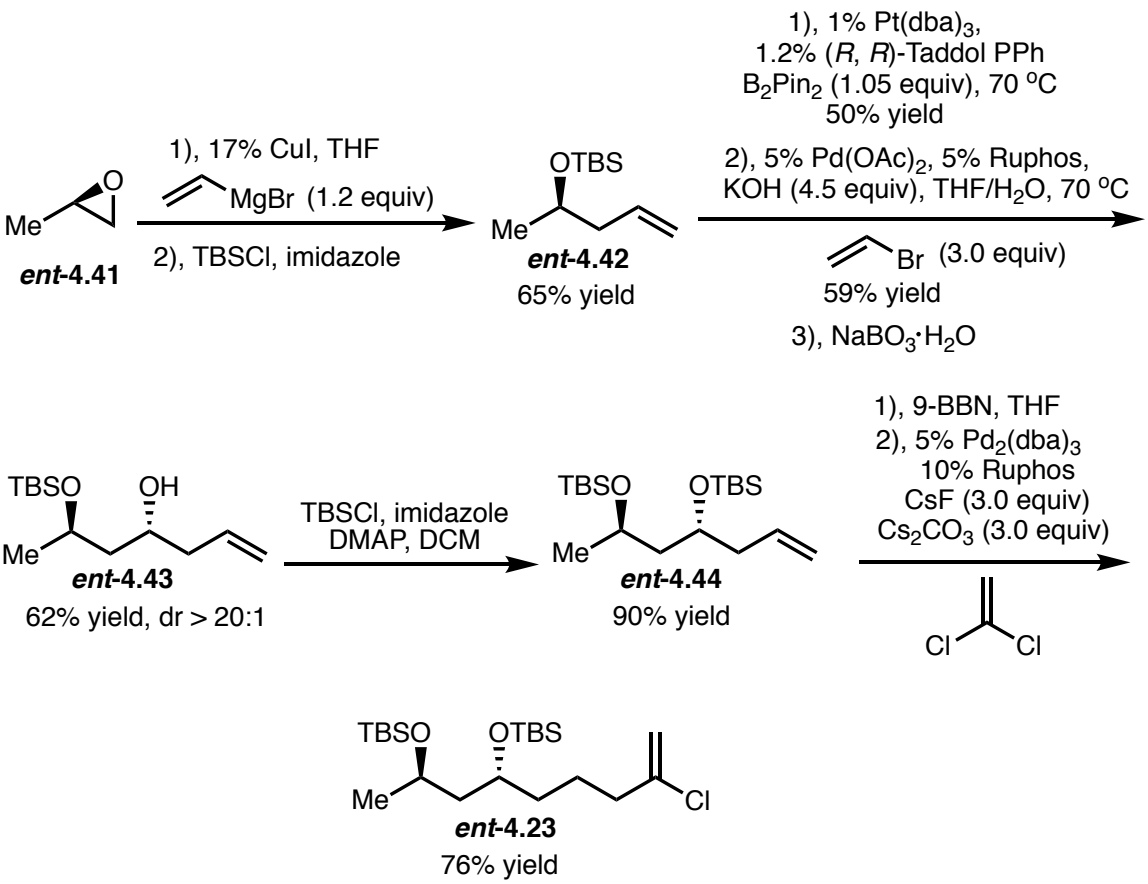


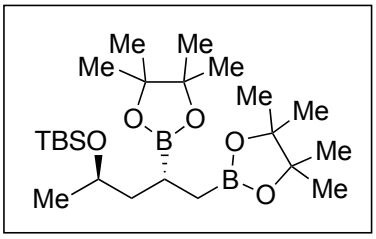
(6*R*,10*R*,14*S*,*E*)-14-((6*S*,8*S*)-6,8-dihydroxy-2-methylenenonyl)-6,10-dihydroxy-8-methyl-12-methyleneoxacyclotetra

dec-7-en-2-one (4.21). The global deprotection was performed according to a previous procedure.[37] To a Teflon vial was added (6*R*,10*R*,14*S*,*E*)-14-((6*S*,8*S*)-6,8-bis((*tert*-butyldimethylsilyl)oxy)-2-methylenenonyl)-6,10-bis((*tert*-butyldimethylsilyl)oxy)-8-methyl-12-methyleneoxacyclotetradec-7-en-2-one **4.49** (4.5 mg, 5 μmol) and THF (0.5 mL). The mixture was cooled to 0 °C, and HF•pyridine (20 μL) was added dropwise into it. Three more portions of HF•pyridine (20 μL) were added slowly into the vial in the following three days at room temperature. Upon completion, the reaction mixture was added carefully into a 20 mL scintillation vial containing saturated $NaHCO_3$ solution (3 mL) at 0 °C, which was then allowed to warm to room temperature and stirred for another twenty minutes. The aqueous layer was extracted with ethyl acetate (5×3 mL). The organic layers were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:10-10:90 hexanes/ethyl acetate, then, 100:10-100:20 hexane/MeOH stain in CAM) to afford **4.21** as a white solid (1.8 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.21 (tt, *J* = 7.5, 4.3 Hz, 1H), 5.09 (d, *J* = 9.3 Hz, 1H), 5.08 (s, 1H), 4.96 (d, *J* = 1.9 Hz, 1H), 4.78 (d, *J* = 1.7 Hz, 1H), 4.72 (s, 1H), 4.37 (ddd, *J* = 10.6, 9.0, 3.4 Hz, 1H), 4.15 (h, *J* = 6.0 Hz, 1H), 3.94 (p, *J* = 6.0 Hz, 1H), 3.84 (tdd, *J* = 10.2, 4.0, 1.8 Hz, 1H), 2.67 (d, *J* = 14.0 Hz, 1H), 2.64 (d, *J* = 14.8 Hz, 4.0 Hz, 1H), 2.42 (dd, *J* =

[37] Paterson, I.; Britton, R.; Delgado, O.; Gardner, N. M.; Meyer, A.; Naylor,G. J.; Poullennec, K. G. *Tetrahedron* **2010**, *66*, 6534-6545.

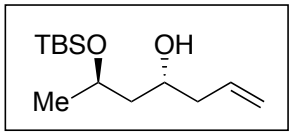
14.3, 3.5 Hz, 1H), 2.32 (dt, *J* = 14.2, 5.9 Hz, 1H), 2.27 – 2.22 (m, 2H), 2.18 – 2.12 (m, 2H), 2.04 (t, *J* = 7.9 Hz, 2H), 1.94 (dd, *J* = 14.1, 10.5 Hz, 1H), 1.89 (dd, *J* = 14.4, 10.0 Hz, 1H), 1.83 – 1.78 (m, 1H), 1.77 (d, *J* = 1.5 Hz, 3H), 1.75 – 1.22 (m, 9H), 1.22 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.42, 145.14, 142.50, 135.76, 129.35, 117.96, 112.62, 71.32, 69.14, 68.70, 68.11, 65.56, 44.60, 44.16, 43.61, 39.46, 38.41, 36.90, 36.54, 35.56, 34.29, 23.67, 23.65, 21.51, 20.14; IR (neat): 3375 (broad, O-H stretch, w), 2924.1 (s), 2869.7 (s), 2854.8 (s), 1731.6 (m), 1716.9 (m), 1556.2 (m), 1488.1 (m), 1456.8 (m), 1436.6 (m), 1380.7 (m), 1296.7 (w), 1243.9 (w), 1142.5 (s), 1075.5 (m), 908.2 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{25}{}^{1}H_{41}{}^{16}O_5$ $[M+H-H_2O]^+$: calculated: 421.2954, found: 421.2955; +5.997° (*c* 0.0667, $CHCl_3$).





(((2*R*,4*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-yl)oxy)(*tert*-butyl)dimethylsilane (*ent*-S4.4) To an oven dried 2-dram vial was added $Pt(dba)_3$ (2.7 mg, 0.003 mmol), (*R,R*)-3,5-di-iso-propylphenyl-TADDOLPPh (2.9 mg, 0.0036 mmol), $B_2(pin)_2$ (80 mg, 0.315 mmol) and THF (0.3 mL) in the glove box. The vial was sealed with Teflon cap, taken outside of the glove box, and heated at 70 °C for twenty minutes. The mixture was cooled to room temperature and returned to the glove box again. The solution was then

charged with (*R*)-*tert*-butyldimethyl(pent-4-en-2-yloxy)silane (60 mg, 0.3 mmol). The vial was then heated at 70 °C outside of the glove box for 12 hours. Upon completion, the yellow solution was extracted with diethyl ether, filtered through a silica gel pipet and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:3 to 100:5 hexanes/ethyl acetate, stain in CAM) to afford ***ent*-S4.4** as a colorless oil (68 mg, 50%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.85 (h, J = 6.2 Hz, 1H), 1.54 (ddd, J = 13.2, 6.5, 5.3 Hz, 1H), 1.46 – 1.37 (m, 1H), 1.22 (s, 24H), 1.18 (t, J = 7.5 Hz, 1H), 1.10 (d, J = 6.0 Hz, 3H), 0.87 (s, 9H), 0.83 (d, J = 7.5 Hz, 2H), 0.04 (d, J = 3.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 82.82, 82.72, 68.27, 43.33, 25.99, 24.89, 24.84, 24.82, 24.76, 23.76, 18.17, -4.37, -4.59; IR (neat): 2977.5 (m), 2929.3 (m), 2857.6 (m), 1370.9 (s), 1315.4 (s), 1254.2 (m), 1141.9 (s), 1070.6 (w), 835.7 (m), 774.2 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{23}{}^{1}H_{49}{}^{11}B_2{}^{16}O_5{}^{28}Si_1$ $[M+H]^+$: calculated: 455.3535, found: 455.3538; $[\alpha]_D$ -0.8° (*c* 1.05, $CHCl_3$).



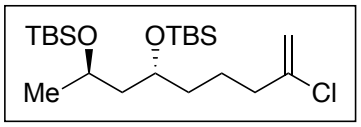
(4*R*,6*R*)-6-((*tert*-butyldimethylsilyl)oxy)hept-1-en-4-ol (***ent*-4.43**) In the glovebox, to an oven dried two dram vial was added $Pd(OAc)_2$ (1.12 mg, 0.005 mmol), Ruphos (2.33 mg, 0.005 mmol), 1,2-bis(boronic) ester **(*ent*-S4.4)** (45.4 mg, 0.1 mmol) and THF (0.35 mL). The vial was taken outside of the glove box, 1M vinyl bromide (0.15 mL, 0.15 mmol) and 8M KOH (56 μL, 0.45 mmol) were added sequentially. The reaction mixture was heated at 70 °C

for 12 hours. Upon completion, the reaction mixture was cooled to room temperature, diluted with diethyl ether, filtered through a silica gel pipet and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:3-100:10 pentane/diethyl ether, stain in CAM) to afford *tert*-butyldimethyl(((2*R*,4*R*)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-6-en-2-yl)oxy)silane **S4.7** as a colorless clear oil (21 mg, 59%, > 20:1 dr). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (ddt, *J* = 17.0, 10.1, 6.9 Hz, 1H), 5.01 (ddt, *J* = 17.1, 2.2, 1.6 Hz, 1H), 4.94 (ddt, *J* = 10.2, 2.3, 1.2 Hz, 1H), 3.81 (ddt, *J* = 13.5, 11.8, 6.1 Hz, 1H), 2.22 – 2.09 (m, 2H), 1.51 – 1.41 (m, 2H), 1.27 – 1.19 (m, overlap, 1H), 1.23 (s, 12H), 1.12 (d, *J* = 6.0 Hz, 3H), 0.88 (d, *J* = 2.7 Hz, 9H), 0.05 (d, *J* = 4.2 Hz, 6H).

To a 20 mL scintillation vial was added boronic ester **S4.7** (260 mg, 0.73 mmol), THF (2 mL) and H_2O (2 mL). The solution was cooled to 0 °C, and then sodium perborate monohydrate (366 mg, 3.67 mmol) was added. The mixture was then allowed to stir overnight. The solution was quenched by H_2O, extracted with diethyl ether, dried over Na_2SO_4 and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:2 – 100:20 pentane/diethyl ether, stain in CAM) to afford ***ent*-4.43** as a colorless clear oil (110 mg, 62%). The spectra were in accordance with a previous report.[38] ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 (ddt, *J* = 17.3,

[38] Amans, D.; Bellosta, V.; Cossy, J. *Org. Lett.* **2007**, *9*, 1453-1456.

10.3, 7.1 Hz, 1H), 5.17 – 5.05 (m, 2H), 4.21 (pd, *J* = 6.1, 3.8 Hz, 1H), 4.02 (dddd, *J* = 9.6, 7.7, 5.2, 2.5 Hz, 1H), 3.30 (d, *J* = 2.3 Hz, 1H), 2.30 – 2.13 (m, 2H), 1.63 (ddd, *J* = 13.9, 9.9, 3.7 Hz, 1H), 1.53 (ddd, *J* = 14.2, 5.5, 2.2 Hz, 1H), 1.22 (d, *J* = 6.3 Hz, 3H), 0.89 (s, 9H), 0.09 (d, *J* = 4.3 Hz, 6H).



(5*R*,7*R*)-5-(4-chloropent-4-en-1-yl)-2,2,3,3,7,9,9,10,10-nonamethyl-4,8-dioxa-3,9-disilaundecane (***ent*-4.23**). Terminal alkene ***ent*-4.43** (110 mg, 0.45 mmol), DCM (2 mL), and imidazole (76.6 mg, 1.12 mmol) were added into a 20 mL scintillation vial sequentially. The mixture was stirred until all solids dissolved, and was then cooled to 0 °C. *tert*-Butyldimethylsilyl chloride (75 mg, 0.5 mmol) was added slowly into the above solution. Lastly, a tip (about 2 mg) of 4-(dimethylamino)pyridine was added. The white slurry was allowed to stir overnight, which was then quenched by water, extracted with DCM and dried over Na_2SO_4. The colorless solution was concentrated *in vacuo* to give a colorless oil. The crude reaction mixture was purified by column chromatography on silica gel (100:0-100:2 pentane/diethyl ether, stain in CAM) to afford (5*R*,7*R*)-5-allyl-2,2,3,3,7,9,9,10,10-nonamethyl-4,8-dioxa-3,9-disilaundecane **(*ent*-4.44)** as a colorless oil (145 mg, 90%).

***ent*-4.23** was prepared according to a previous literature with slightly modification.[39] In the glove box, to an oven dried four-dram vial were added 9-BBN dimer (48.8 mg, 0.2 mmol), THF (1 mL) and ***ent*-4.44** (145 mg, 0.4 mmol). The mixture was allowed to stir for 1.5 hours to resulting in yellow clear solution. $Pd_2(dba)_3$ (18.3 mg, 0.02 mmol), Ruphos (18.7 mg, 0.04 mmol), THF (3 mL), CsF (182.3 mg, 1.2 mmol) and Cs_2CO_3 (391 mg, 1.2 mmol) were added sequentially into the solution. The vial was sealed with a Teflon cap and taken outside of the glove box. 1,1-Dichloroethylene (0.128 mL, 1.6 mmol) was added into the reaction solution. The solution was then heated at 70 °C for 12 hours. Upon completion, the reaction mixture was diluted with diethyl ether, filtered through a silica gel pipet and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:2-100:3 pentane/diethyl ether, stain in CAM) to afford ***ent*-4.23** as a colorless clear oil (128 mg, 76 %). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.14 (d, J = 1.2 Hz, 1H), 5.11 (t, J = 1.2 Hz, 1H), 3.88 (h, J = 6.3 Hz, 1H), 3.76 (p, J = 6.7 Hz, 1H), 2.32 (t, J = 7.4 Hz, 2H), 1.67 – 1.56 (m, 3H), 1.53 – 1.38 (m, 3H), 1.14 (dd, J = 6.1, 1.2 Hz, 3H), 0.88 (s, 18H), 0.09 – 0.02 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.90, 111.87, 69.77, 66.34, 47.88, 39.19, 36.61, 25.91, 24.51, 22.63, 18.08, -3.88, -4.12, -4.23, -4.48; IR (neat): 2954.0 (m), 2928.9 (m), 2886.8 (w), 2856.6 (m), 1472.1 (w), 1374.7 (w), 1253.2 (m), 1118.0 (m), 1061.8 (m), 1004.8 (m), 938.9 (w),

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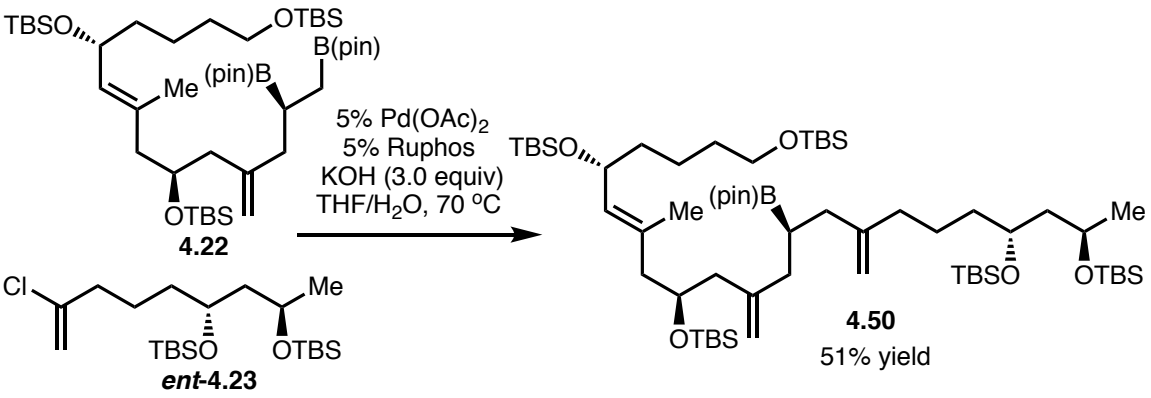
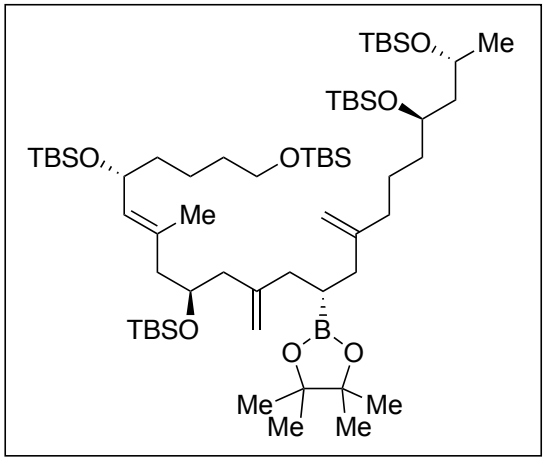
[39] Liron, F.; Fosse, C.; Pernolet, A.; Roulland, E. *J. Org. Chem.*, **2007**, *72*, 2220-2223.

878.0 (m), 832.4 (s), 805.5 (s), 770.9 (s), 703.6 (w), 663.4 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{21}{}^{1}H_{46}{}^{35}Cl_{1}{}^{16}O_{2}{}^{28}Si_{2}$ $[M+H]^{+}$: calculated: 421.2725, found: 421.2745; $[\alpha]_D$ -7.0° (*c* 1.16, $CHCl_3$).



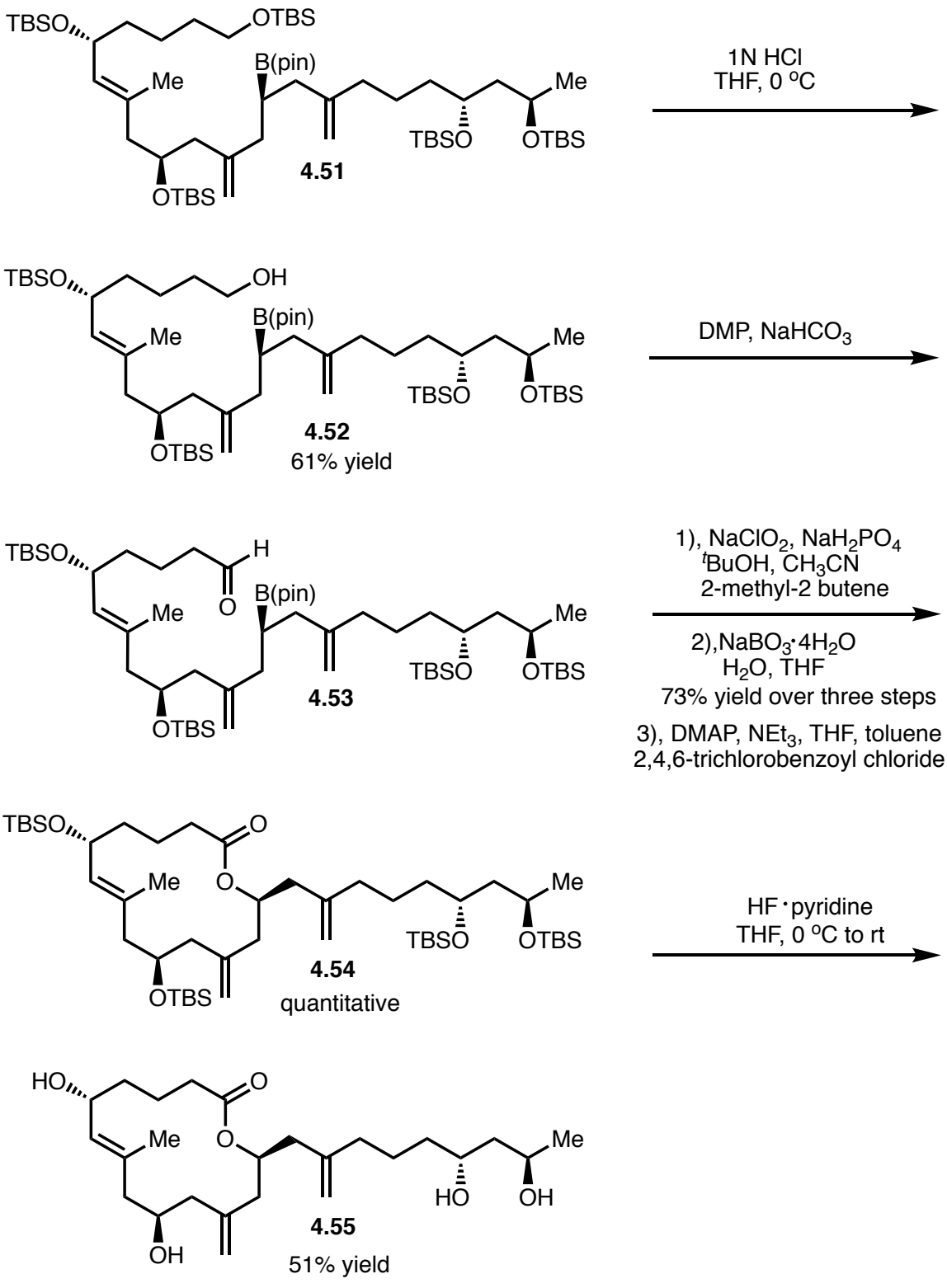


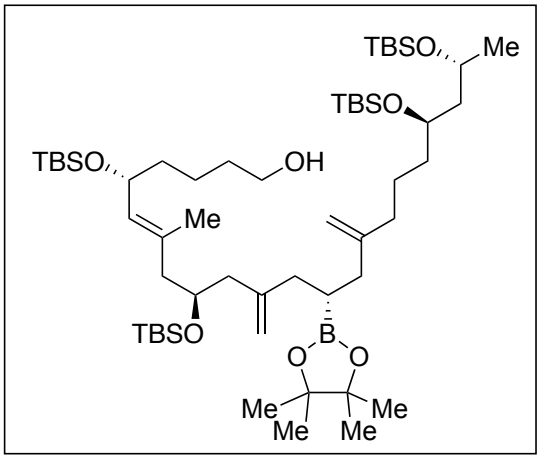
(9*R*,13*R*,17*S*,23*R*,25*R*,*E*)-9,13,23-tris((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,11,25,27,27,28,28-decamethyl-15,19-dimethylene-17-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,26-dioxa-3,27-disilanonacos-10-ene. (4.50) The reaction was performed

according to a previous procedure[40] with slightly modification. In the glove box, an oven dried 20 mL vial was added $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), Ruphos (14 mg, 0.03 mmol) and THF (3 mL). The mixture was allowed to stir for 5 minutes before adding **4.22** (260 mg, 0.3 mmol) and ***ent*-4.23** (128 mg, 0.3 mmol) sequentially. The vial was sealed and taken outside of the glove box. Degassed 8M KOH (0.17 mL, 1.35 mmol) and degassed H_2O (0.3 mL) were added into the vial. The mixture was then heated at 70 °C overnight. The solution changed color from orange red to black. The reaction mixture was extracted by diethyl ether, dried over Na_2SO_4 and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:0.5-100:5 hexanes/ethyl acetate, stain in CAM) to afford **4.50** as a colorless oil (152 mg, 51%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.16 (d, J = 8.5 Hz, 1H), 4.84 (s, 1H), 4.75 (s, 1H), 4.74 (s, 1H), 4.69 (s, 1H), 4.31 (td, J = 7.9, 4.6 Hz, 1H), 3.94 – 3.85 (m, 2H), 3.74 (p, J = 5.4 Hz, 1H), 3.59 (t, J = 6.6 Hz, 2H), 2.19 – 2.00 (m, 8H), 2.01 – 1.95 (m, 2H), 1.61 (s, 3H), 1.66 – 1.58 (m, overlap, 1H), 1.54 – 1.23 (m, 12H), 1.18 (s, 12H), 1.14 (dd, J = 6.0, 1.2 Hz, 3H), 0.91 – 0.83 (m, 45H), 0.08 – -0.03 (m, 30H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 149.09, 146.50, 132.46, 131.46, 112.16, 109.41, 82.89, 70.22, 70.05, 69.66, 66.35, 63.27, 48.00, 47.49, 43.98, 38.46, 38.27, 37.83, 37.59, 36.12, 32.87, 25.99, 25.95, 25.93, 25.90, 24.87, 24.81, 24.53, 23.16, 21.86, 19.90, 18.38, 18.20, 18.10, 18.06, 16.94, -3.88, -4.01, -4.14, -4.21,

[40] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386-390.

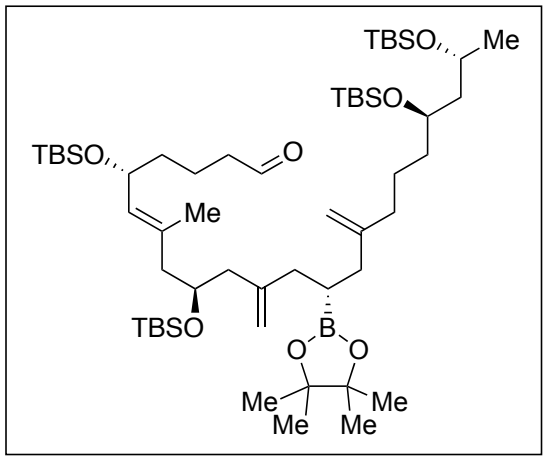
-4.36, -4.45, -4.75, -5.27; IR (neat): 2953.6 (m), 2928.5 (m), 2856.4 (m), 1471.9 (w), 1462.1 (w), 1380.0 (w), 1361.2 (w), 1252.8 (m), 1144.1 (m), 1090.8 (m), 1064.9 (m), 1005.1 (w), 938.6 (w), 890.9 (w), 832.9 (s), 807.0 (m), 772.1 (s), 665.1 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{61}{}^{1}H_{131}{}^{11}B_{1}{}^{16}O_{7}{}^{14}N_{1}{}^{28}Si_{5}$ $[M+NH_4]^+$: calculated: 1140.8865, found: 1140.8897; $[\alpha]_D$ +1.1° (*c* 1.63, $CHCl_3$).


TBSO
OTBS
B(pin)
Me
Me
TBSO
OTBS
OTBS
4.51
1N HCl
THF, 0 °C
TBSO
OH
B(pin)
Me
Me
TBSO
OTBS
OTBS
4.52
61% yield
DMP, NaHCO3
TBSO
H
O
B(pin)
Me
Me
TBSO
OTBS
OTBS
4.53
1), NaClO2, NaH2PO4
tBuOH, CH3CN
2-methyl-2 butene
2),NaBO3·4H2O
H2O, THF
73% yield over three steps
3), DMAP, NEt3, THF, toluene
2,4,6-trichlorobenzoyl chloride
TBSO
O
Me
O
Me
TBSO
OTBS
OTBS
4.54
quantitative
HF·pyridine
THF, 0 °C to rt
HO
O
Me
O
Me
HO
OH
OH
4.55
51% yield



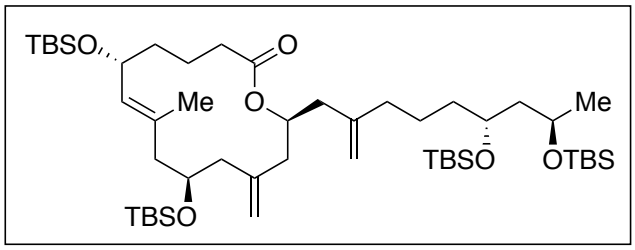
(5*R*,9*R*,13*S*,19*R*,21*R*,*E*)-5,9,19,21-tetrakis((*tert*-butyldimethylsilyl)oxy)-7-methyl-11,15-dimethylene-13-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)docos-6-en-1-ol (4.52). A 20 mL scintillation vial was charged with **4.51** (60 mg, 0.06 mmol) and THF (6 mL). The solution was cooled to 0 °C, and allowed to stir at 0 °C for 15 minutes. HCl (0.06 mL, 1 M, 0.06 mmol) was added dropwise into the mixture, and the mixture was allowed to stir at 4 °C (cold room) overnight. The vial was cooled to 0 °C again, and then quenched by adding one pipet of saturated $Na_2S_2O_3$ (0.5 mL). The reaction mixture was extracted with diethyl ether, filtered through a $Na_2S_2O_4$ pipet and evaporated *in vacuo*. The crude reaction mixture was then purified by column chromatography on silica gel (100:2-80:20 hexanes/ethyl acetate, stain in CAM) to afford **4.52** as a clear colorless oil (32.3 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.16 (d, *J* = 8.5 Hz, 1H), 4.84 (s, 1H), 4.75 (s, 1H), 4.74 (s, 1H), 4.70 (s, 1H), 4.33 (td, *J* = 7.9, 4.5 Hz, 1H), 3.92 (p, *J* = 5.9 Hz, 1H), 3.88 (h, *J* = 6.0 Hz, 1H), 3.75 (p, *J* = 5.5 Hz, 1H), 3.63 (q, *J* = 6.1 Hz, 2H), 2.18 – 2.01 (m, 8H), 1.97 (q, *J* = 7.3 Hz, 2H), 1.62 (s, 3H), 1.59 – 1.23 (m, 13H), 1.18 (s, 12H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.92 – 0.82 (m, 36H), 0.12 – -0.04 (m, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 149.10, 146.46, 132.21, 131.78, 112.22, 109.42, 82.93, 70.25, 70.07, 69.52, 66.37, 62.97, 48.00, 47.46, 43.91, 38.46, 38.19, 37.83, 37.60, 36.14, 32.80, 29.70,

25.96, 25.90, 24.87, 24.81, 24.54, 23.17, 21.59, 19.95, 18.21, 18.11, 18.08, 17.09, -3.87, -4.00, -4.12, -4.20, -4.37, -4.44, -4.74; IR (neat): 2952.7 (m), 2928.4 (s), 2856.4 (m), 1472.1 (w), 1462.1 (w), 1380.1 (m), 1361.5 (w), 1253.4 (m), 1144.2 (m), 1086.9 (m), 1064.2 (m), 1005.2 (w), 938.7 (w), 891.5 (w), 834.3 (s), 806.8 (m), 773.2 (w) cm^{-1}; HRMS-(DART+) for $^{12}C_{55}{}^{1}H_{117}{}^{11}B_{1}{}^{16}O_{7}{}^{14}N_{1}{}^{28}Si_{4}$ $[M+NH_4]^+$: calculated: 1026.8000, found: 1026.8042; $[\alpha]_D$ +1.4° (*c* 1.33, $CHCl_3$).



(5*R*,9*R*,13*S*,19*R*,21*R*,*E*)-5,9,19,21-tetrakis((*tert*-butyldimethylsilyl)oxy)-7-methyl-11,15-dimethylene-13-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)docos-6-enal (4.53) To a 20 mL scintillation vial was added **(4.52)** (10 mg, 9.9 μmol) and DCM (1 mL). The mixture was cooled to 0 °C, Dess-Martin periodinane (5 mg, 11.9 μmol) and $NaHCO_3$ (4.2 mg, 49.6 μmol) were added. After 4 hours, the reaction mixture was concentrated *in vacuo*, then extracted with 1:1 hexane/Et_2O, filtered through a silica gel padded sintered funnel, and then rinsed with 1:1 hexane/Et_2O, and evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:2-100:3 hexanes/ethyl acetate, stain in CAM) to afford **4.53** as a clear colorless oil (8 mg, 80%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.75 (td, *J* = 1.0, 1.0 Hz, 1H), 5.16 (d, *J* =

8.1 Hz, 1H), 4.84 (s, 1H), 4.75 (s, 1H), 4.74 (s, 1H), 4.70 (s, 1H), 4.34 (td, *J* = 7.9, 4.8 Hz, 1H), 3.92 (p, *J* = 5.8 Hz, 1H), 3.88 (h, *J* = 5.9 Hz, 1H), 3.74 (p, *J* = 5.5 Hz, 1H), 2.41 (tt, *J* = 7.3, 1.4 Hz, 2H), 2.20 – 2.00 (m, 8H), 1.97 (q, *J* = 7.8 Hz, 2H), 1.73 (tdd, *J* = 12.8, 10.3, 6.1 Hz, 1H), 1.68 – 1.57 (m, 1H), 1.62 (s, 3H), 1.52 – 1.44 (m, 1H), 1.45 – 1.23 (m, 7H), 1.21 (td, *J* = 6.5, 5.9, 1.3 Hz, 1H), 1.18 (s, 12H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.91 – 0.83 (m, 36H), 0.10 – -0.03 (m, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 202.64, 149.09, 146.42, 132.17, 131.82, 112.23, 109.42, 82.91, 70.13, 70.06, 69.26, 66.36, 48.01, 47.43, 44.06, 43.85, 38.44, 37.82, 37.78, 37.60, 36.15, 29.70, 25.96, 25.94, 25.87, 24.88, 24.82, 24.54, 23.17, 19.89, 18.27, 18.16, 18.11, 18.07, 16.96, -3.87, -4.00, -4.10, -4.20, -4.33, -4.45, -4.46, -4.79; IR (neat): 2953.4 (m), 2928.5 (s), 2856.4 (m), 1731.6 (w), 1472.3 (w), 1462.1 (w), 1380.0 (m), 1361.8 (m), 1253.5 (m), 1144.3 (m), 1088.1 (m), 1065.32 (m), 1005.4 (w), 971.1 (w), 938.7 (w), 890.7 (w), 834.5 (s), 807.7 (m), 773.5 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{55}{}^{1}H_{115}{}^{11}B_{1}{}^{16}O_{7}{}^{14}N_{1}{}^{28}Si_{4}$ $[M+NH_4]^+$: calculated: 1024.7844, found: 1024.7869. $[\alpha]_D$ +2.1° (*c* 0.14, $CHCl_3$).



(6*R*,10*R*,14*S*,*E*)-14-((6*R*,8*R*)-6,8-bis(
(*tert*-butyldimethylsilyl)oxy)-2-met
hylenenonyl)-6,10-bis((*tert*-butyldi
methylsilyl)oxy)-8-methyl-12-meth

yleneoxacyclotetradec-7-en-2-one (4.54).

(5*R*,9*R*,13*S*,19*R*,21*R*,*E*)-5,9,19,21-tetrakis((*tert*-butyldimethylsilyl)oxy)-7-methyl-11,15-dimethylene-13-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)docos-6-enoic acid **S4.8** was prepared according to a previous procedure[41] with slightly modification. A 20 mL scintillation vial was charged with aldehyde **4.53** (32 mg, 31.8 μmol), ^{t}BuOH (1 mL), CH_3CN (1 mL) and 2- methyl-2-butene (0.75 mL, 2.2 mmol) sequentially. The vial was then cooled to 0 °C. A solution of $NaClO_2$ (28.8 mg, 0.32 mmol) and NaH_2PO_4 (43.6 mg, 0.32 mmol) in H_2O (1 mL) was added into the vial. The solution was then allowed to warm up to room temperature and stir for four hours. The reaction mixture was quenched by H_2O, extracted with diethyl ether, then filtered through a $Na_2S_2O_4$ pipet and evaporated *in vacuo*. The crude reaction mixture was then purified by column chromatography on silica gel (100:6-60:40 hexanes/ethyl acetate, stain in CAM) to afford **S4.8** as a clear colorless oil (48 mg, quantitative, with slight impurity) which was used directly in the next step.

To a 20 mL scintillation vial were added carboxylic acid **S4.8** (48 mg, 47.7 μmol), THF (2 mL) and H_2O (2 mL). The solution was cooled to 0 °C, and treated with sodium perborate tetrahydrate (220 mg, 1.43 mmol). The mixture was then allowed to stir

[41] Paterson, I.; Paquet, T. *Org. Lett.* **2010**, *12*, 2158-2161.

overnight. The solution was quenched by H_2O, extracted with diethyl ether, dried over Na_2SO_4, evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:0 – 100:20 hexanes/ethyl acetate, stain in CAM) to afford (5*R*,9*R*,13*S*,19*R*,21*R*,*E*)-5,9,19,21-tetrakis((*tert*-butyldimethylsilyl)oxy)-13-hydroxy-7-methyl-11,15-dimethylenedocos-6-enoic acid **S4.9** as a colorless oil (21.5 mg, 73 % over three steps).

The Yamaguchi esterification was performed according to a previous procedure.[42] To an oven dried 20 mL scintillation vial (charged with stirring bar, cooled under vacumn) was added (5*R*,9*R*,13*S*,19*S*,21*S*,*E*)-5,9,19,21-tetrakis((*tert*-butyldimethylsilyl)oxy)-13-hydroxy-7-methyl-11,15-dimethylenedocos-6-enoic acid **S4.9** (21.5 mg, 23.5 μmol), THF (3 mL), triethyl amine (23.8 mg, 235 μmol) and 2,4,6-trichlorobenzoylchloride (34.4 mg, 141 μmol). The solution was allowed to stir at room temperature for two hours before toluene (20 mL) was added. The solution was transferred into a syringe. The above solution was added into an oven dried 100 mL round bottom flask (precharged with DMAP (34.5 mg, 282 μmol) and toluene (24 mL)) *via* syringe pump at 80°C over nine hours. The solution was heated at 80°C overnight, which was then cooled to room temperature and

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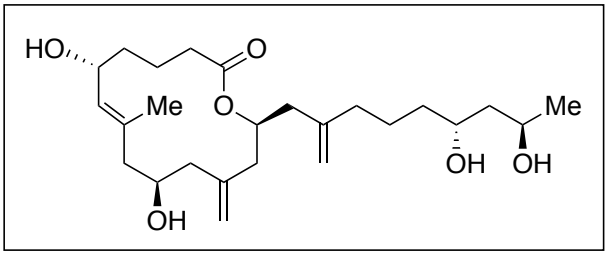
[42] Williams, D. R.; Patnaik, S.; Plummer, S. V. *Org. Lett.* **2003**, *5*, 5035-5038.

evaporated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:0-100:2 hexanes/ethyl acetate, stain in CAM) to afford **4.54** as clear colorless oil (23 mg, quantitative).

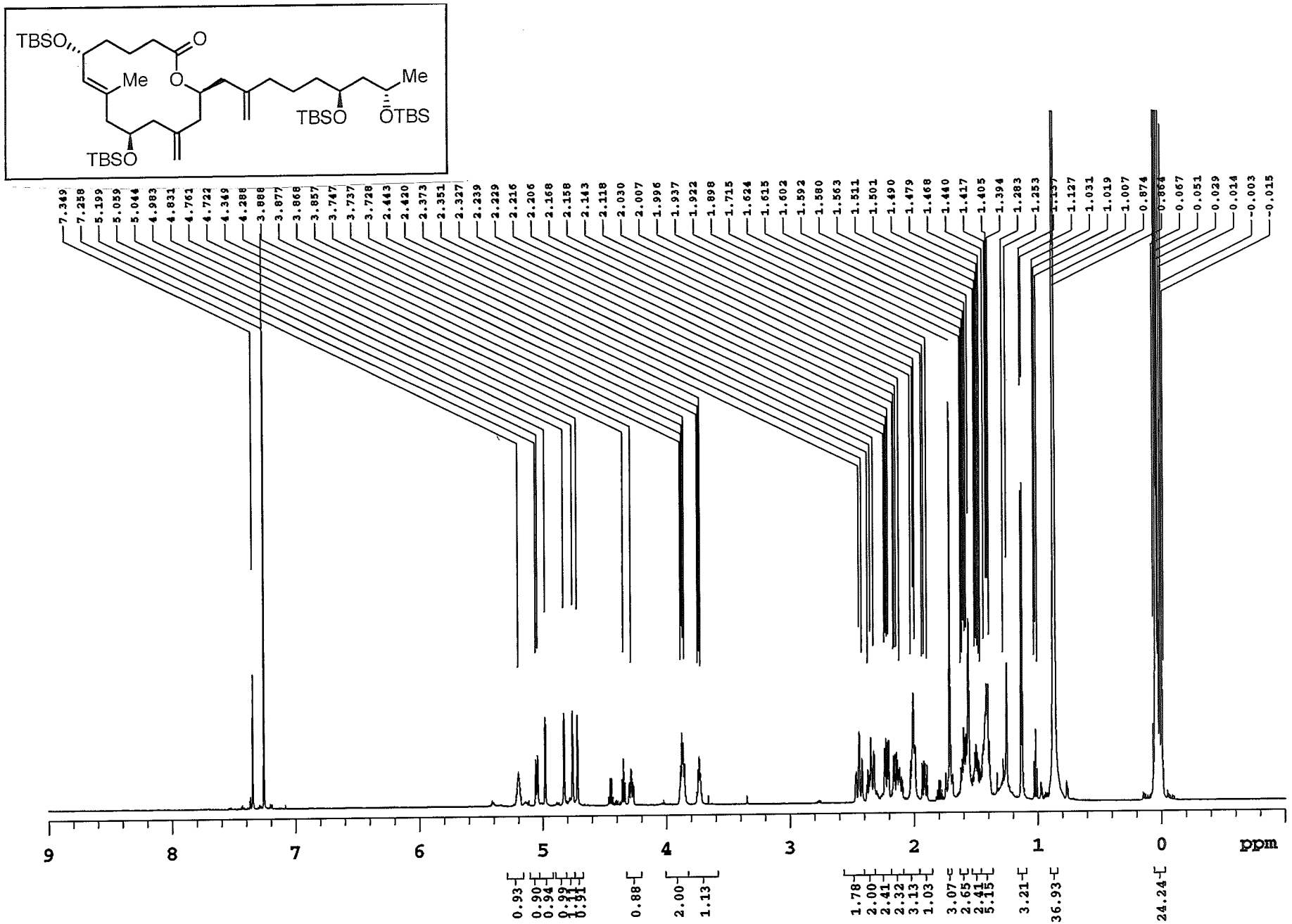
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.23 – 5.17 (m, 1H), 5.05 (d, *J* = 8.7 Hz, 1H), 4.98 (s, 1H), 4.83 (d, *J* = 2.1 Hz, 1H), 4.76 (d, *J* = 1.6 Hz, 1H), 4.72 (s, 1H), 4.29 (ddd, *J* = 10.2, 8.7, 3.2 Hz, 1H), 3.94 – 3.82 (m, 2H), 3.77 – 3.69 (m, 1H), 2.45 (t, *J* = 14.2 Hz, 2H), 2.36 – 2.29 (m, 2H), 2.23 (dd, *J* = 14.1, 6.0 Hz, 2H), 2.18 – 2.12 (m, 2H), 2.02 (tt, *J* = 9.0, 4.6 Hz, 3H), 1.92 (dd, *J* = 14.0, 9.0 Hz, 1H), 1.72 (d, *J* = 1.3 Hz, 3H), 1.64 – 1.57 (m, 2H), 1.53 –1.37 (m, 5H), 1.33 – 1.19 (m, 3H), 1.14 (d, *J* = 6.1 Hz, 3H), 0.92 – 0.83 (m, 36H), 0.10 – -0.04 (m, 24H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.34, 145.71, 141.94, 132.96, 130.73, 127.99, 117.54, 111.95, 71.68, 71.16, 70.02, 69.24, 66.36, 47.98, 46.66, 43.47, 39.71, 39.12, 38.16, 37.43, 35.94, 34.83, 25.93, 25.86, 24.49, 23.11, 21.29, 20.11, 18.19, 18.14, 18.10, -3.90, -4.07, -4.21, -4.36, -4.39, -4.47, -4.67, -4.77; IR (neat): 2954.5 (s), 2928.2 (s), 2856.3 (s), 1734.0 (m), 1472.4 (m), 1458.4 (m), 1253.7 (s), 1087.0 (m), 1050.5 (m), 835.2 (s), 806.7 (m), 807.9 (w), 774.0 (s) cm^{-1}; HRMS-(DART+) for $^{12}C_{49}{}^{1}H_{98}{}^{16}O_6{}^{28}Si_4{}^{23}Na_1$ $[M+Na]^+$: calculated: 917.6338, found: 917.6335; $[\alpha]_D$ +2.4° (*c* 0.72, $CHCl_3$).



(6*R*,10*R*,14*S*,*E*)-14-((6*R*,8*R*)-6,8-dihydroxy-2-methylenenonyl)-6,10-dihydroxy-8-methyl-12-methyleneoxacyclotetradec-7-en-2-one (4.55) The global deprotection was performed according to a previous procedure.[43] To a Teflon vial was added **4.54** (4 mg, 4.5 μmol) and THF (0.5 mL). The solution was cooled to 0 °C and HF•pyridine (18 μL) was added dropwise into it. Three more portions of HF•pyridine (13 μL) were added slowly in the following three days at room temperature. Upon completion, the reaction mixture was added carefully into a 20 mL scintillation vial containing 2.2 mL saturated $NaHCO_3$ solution at 0 °C, after which the solution was then allowed to warm to room temperature and stirred for another twenty minutes. The aqueous layer was extracted with ethyl acetate (5×3 mL). The organic layers were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (100:10-10:90 hexanes/ethyl acetate, then, 100:10-100:20 DCM/MeOH stain in CAM) to afford **4.55** as a white solid (1 mg, 51%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.20 (tt, *J* = 7.7, 3.8 Hz, 1H), 5.10 (d, *J* = 12.1 Hz, 1H), 5.09 (s, 1H), 4.96 (s, 1H), 4.79 (s, 1H), 4.72 (s, 1H), 4.37 (td, *J* = 10.4, 3.3 Hz, 1H), 4.15 (h, *J* = 6.0 Hz, 1H), 3.96 (p, *J* = 5.8 Hz, 1H), 3.84 (t, *J* = 9.1 Hz, 1H), 2.68

[43] Paterson, I.; Britton, R.; Delgado, O.; Gardner, N. M.; Meyer, A.; Naylor,G. J.; Poullennec, K. G. *Tetrahedron* **2010**, *66*, 6534-6545.

(d, J = 14.2 Hz, 1H), 2.64 (dd, J = 13.5, 4.4 Hz, 1H), 2.43 (dd, J = 14.3, 3.5 Hz, 1H), 2.35 – 2.30 (m, 1H), 2.30 – 2.22 (m, 2H), 2.19 – 2.12 (m, 2H), 2.12 – 2.07 (m, 1H), 2.05 – 1.97 (m, 1H), 1.94 (dd, J = 14.0, 10.5 Hz, 1H), 1.89 (dd, J = 14.4, 10.0 Hz, 1H), 1.84 – 1.79 (m, 1H), 1.77 (d, J = 1.4 Hz, 3H), 1.72 – 1.36 (m, 9H), 1.22 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.53, 145.16, 142.51, 135.77, 129.33, 117.96, 112.72, 71.41, 68.80, 68.71, 68.11, 65.54, 44.61, 44.23, 43.60, 39.48, 38.39, 36.84, 36.58, 35.25, 34.35, 23.62, 23.58, 21.50, 20.13; IR (neat): 3385.4 (broad, O-H stretch, m), 2924.3 (s), 2853.3 (m), 1731.8 (s), 1716.0 (m), 1557.3 (s), 1488.6 (s), 1456.4 (s), 1435.5 (s), 1418.3 (s), 1386.8 (m), 1289.3 (m), 1243.9 (m), 1154.9 (m), 1077.0 (m) cm^{-1}; HRMS-(DART+) for $^{12}C_{25}{}^{1}H_{42}{}^{16}O_6{}^{23}Na_1$ $[M+Na]^+$: calculated: 461.2879, found: 461.2868; $[\alpha]_D$ -7.49° (*c* 0.0267, $CHCl_3$).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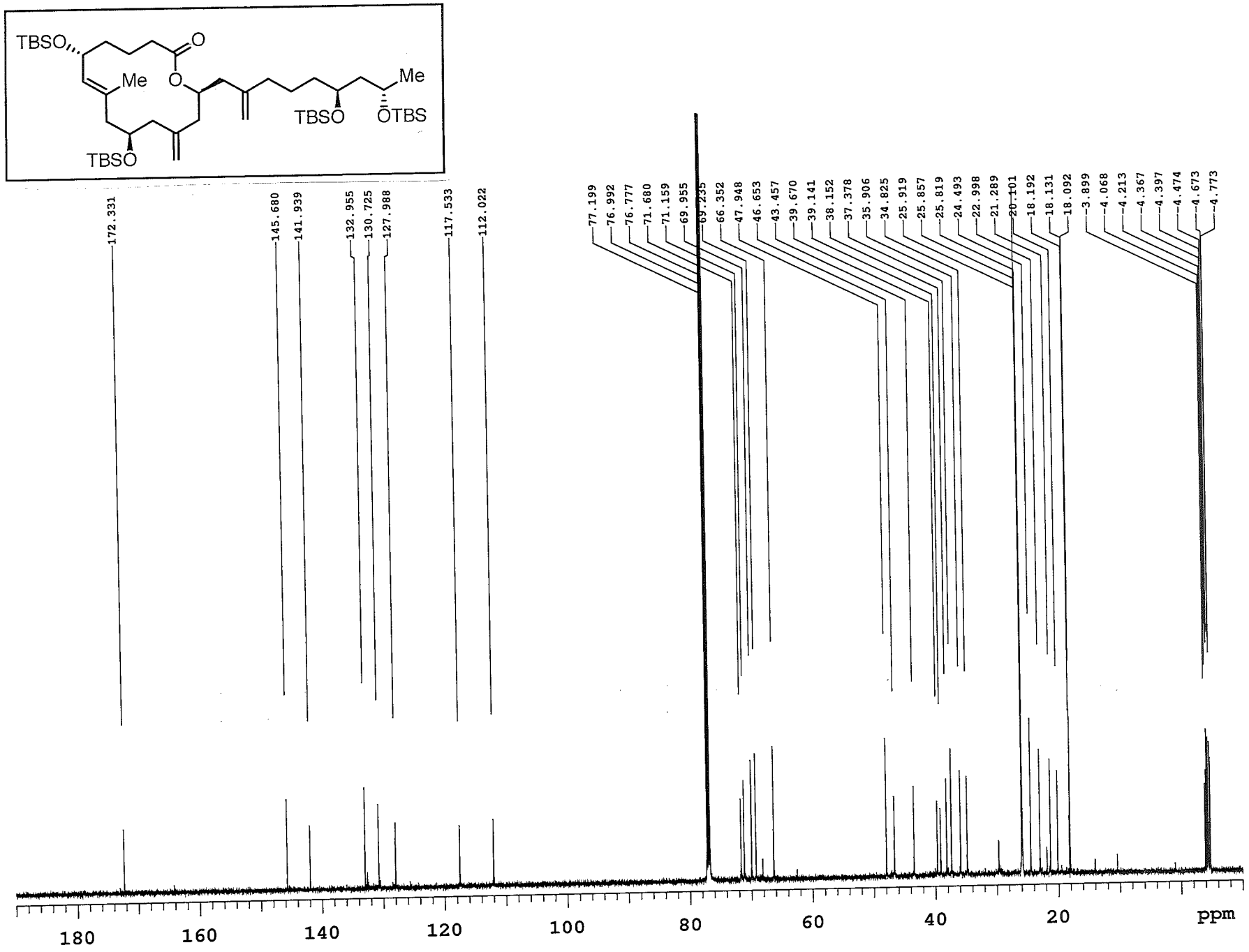
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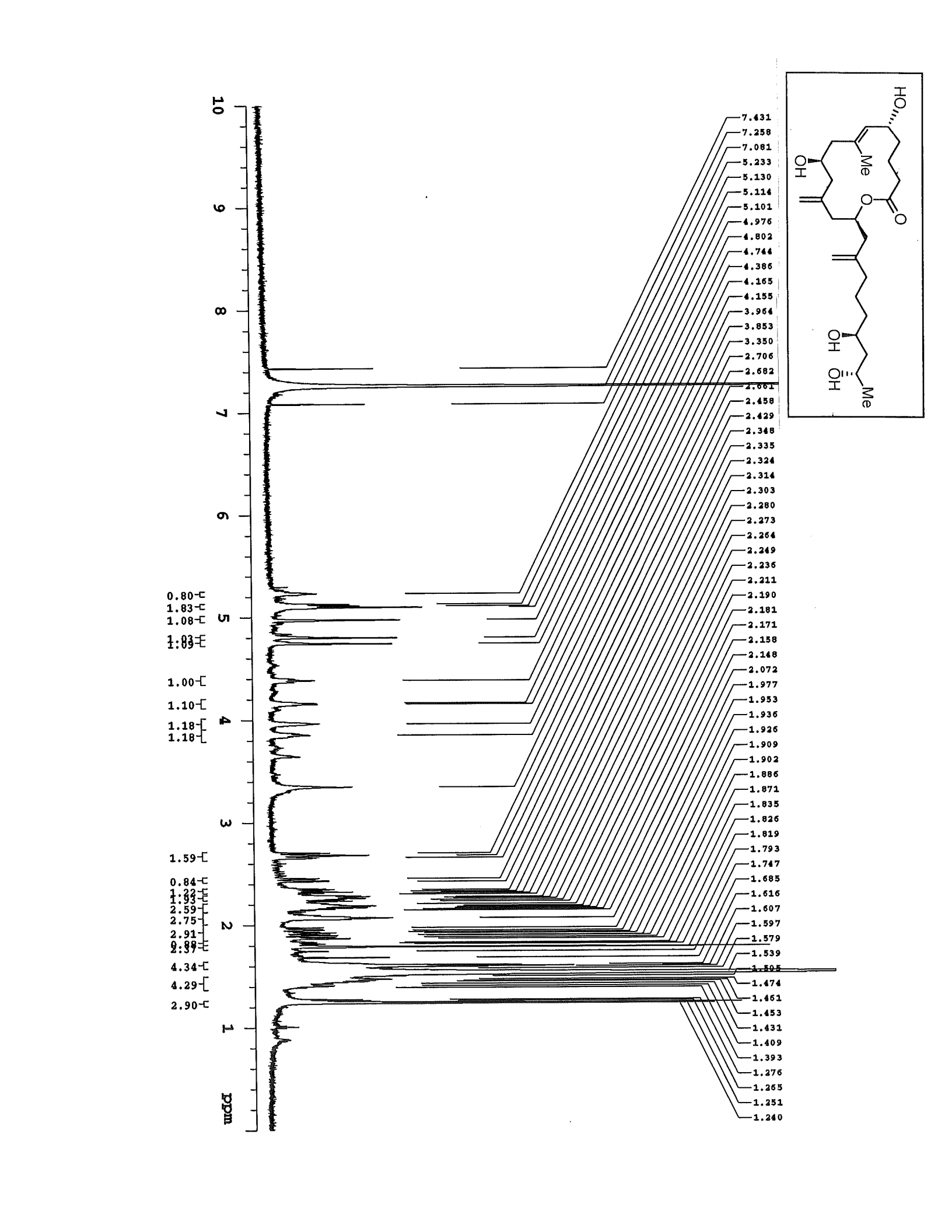
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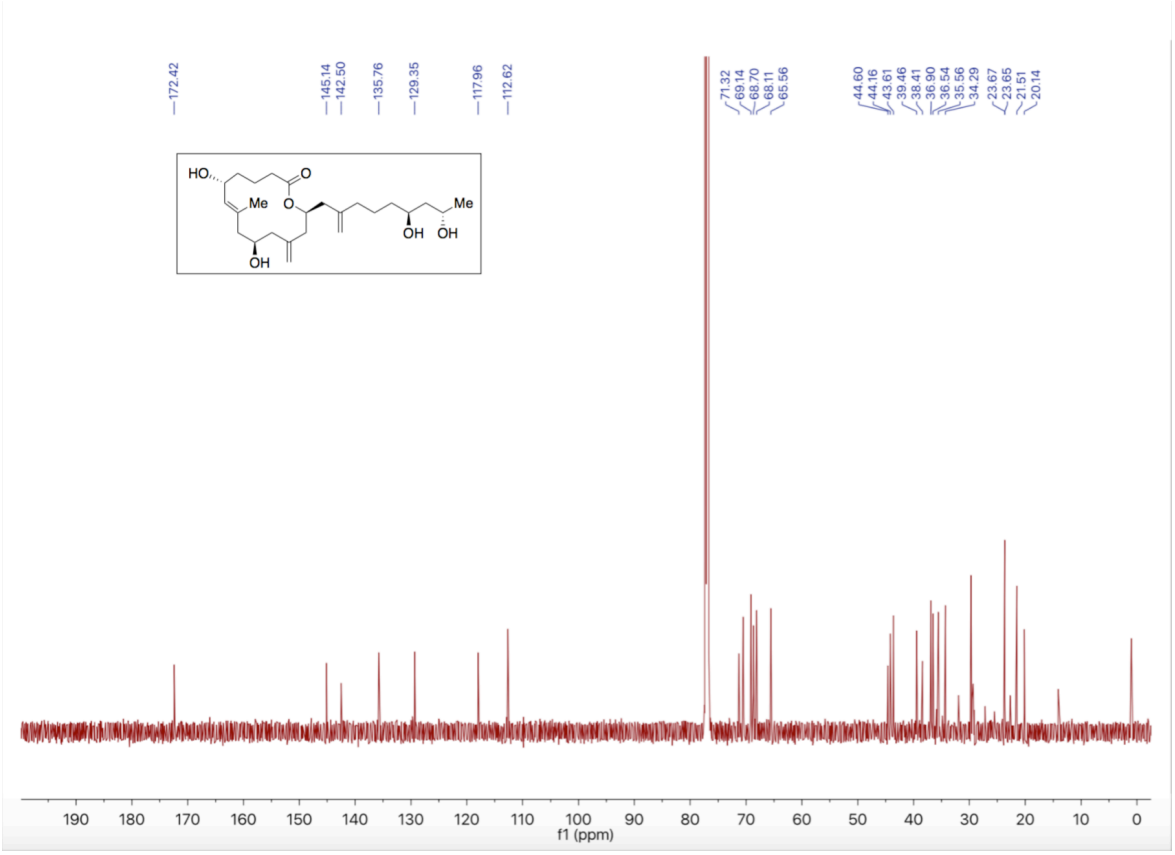
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23.65
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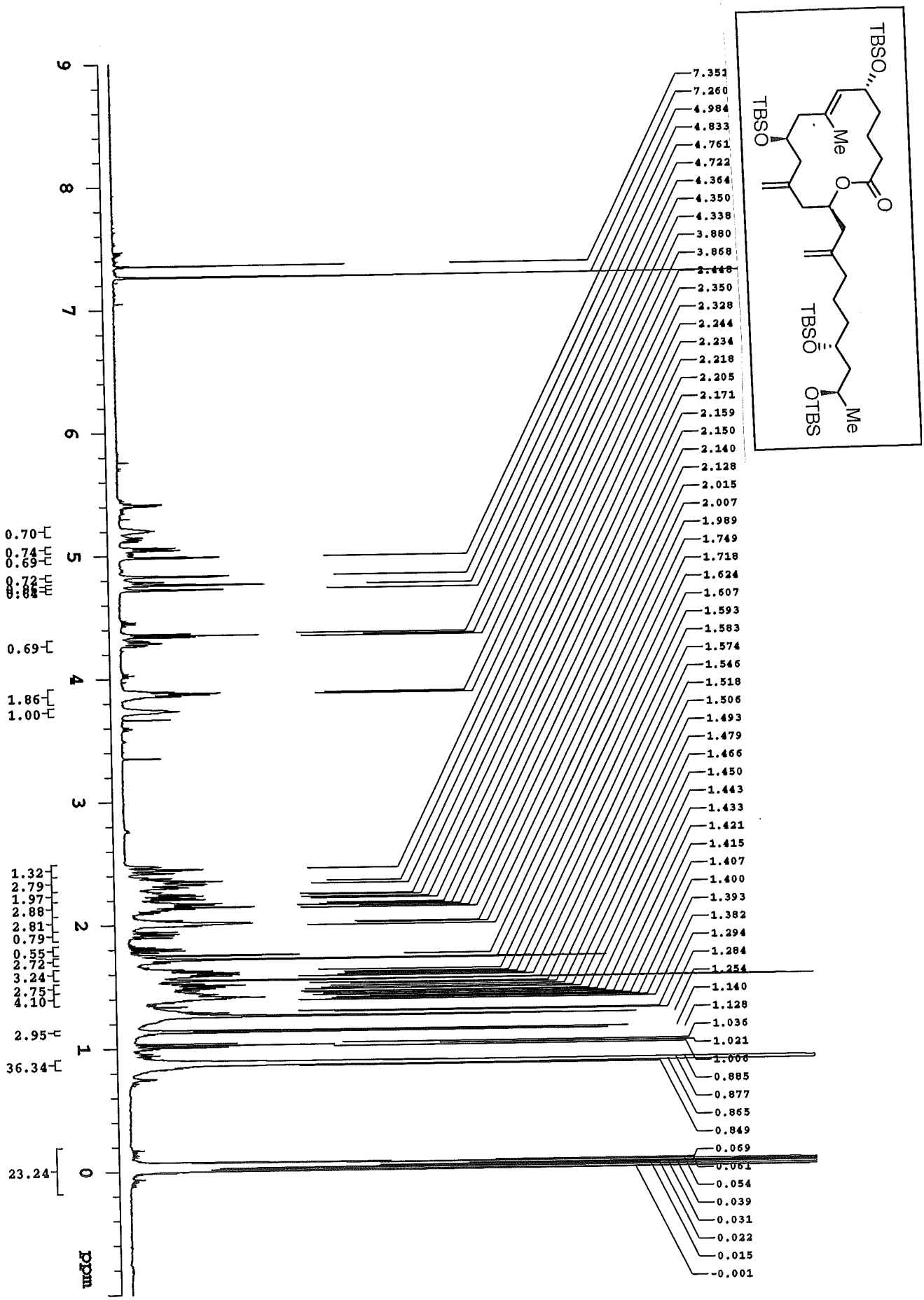
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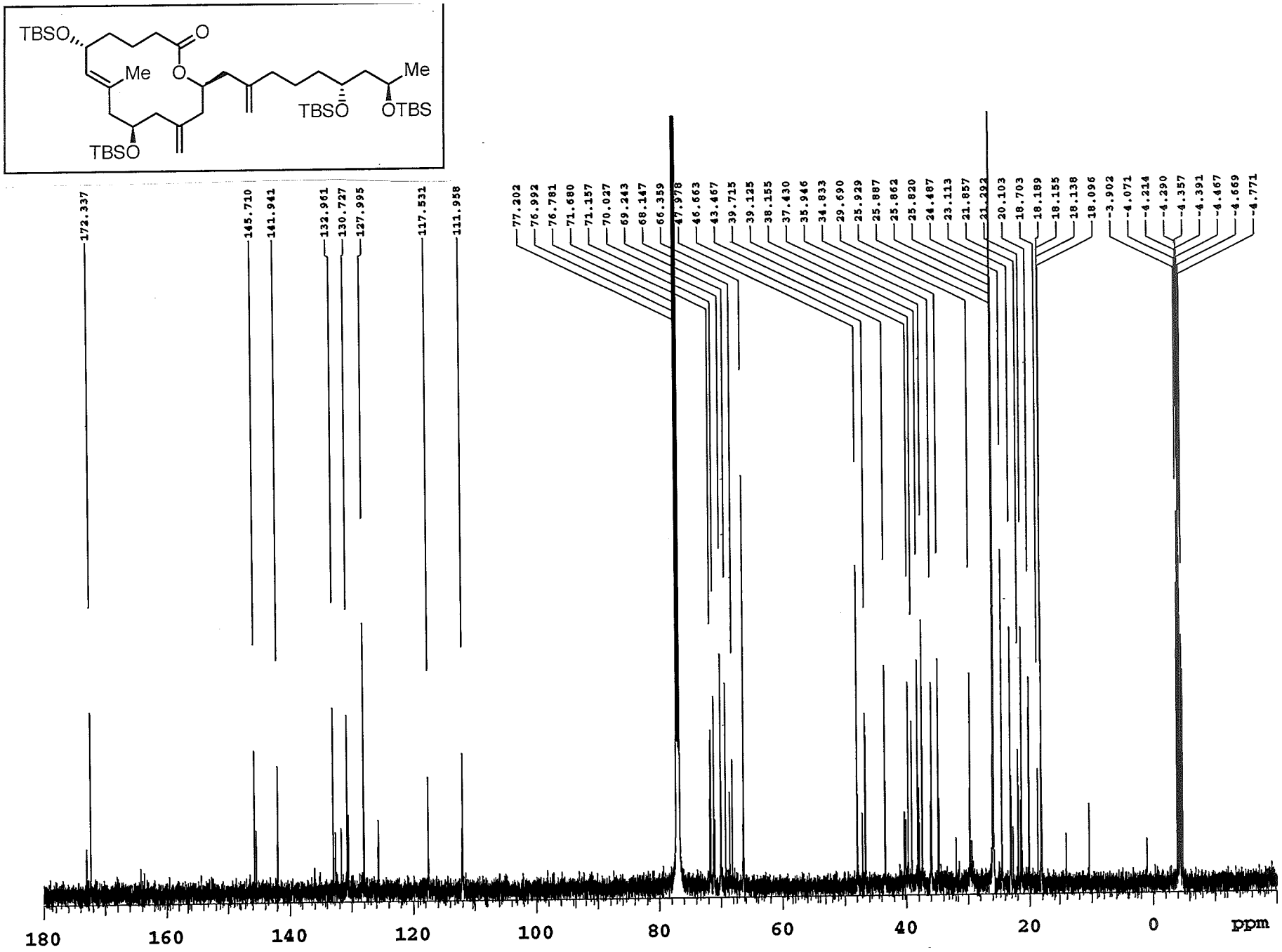
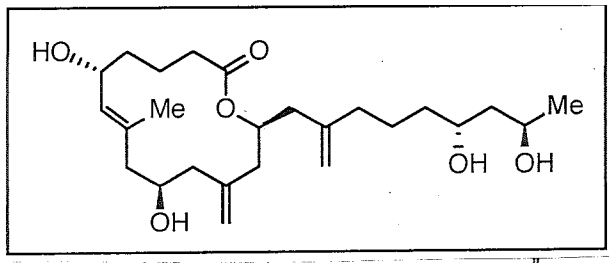
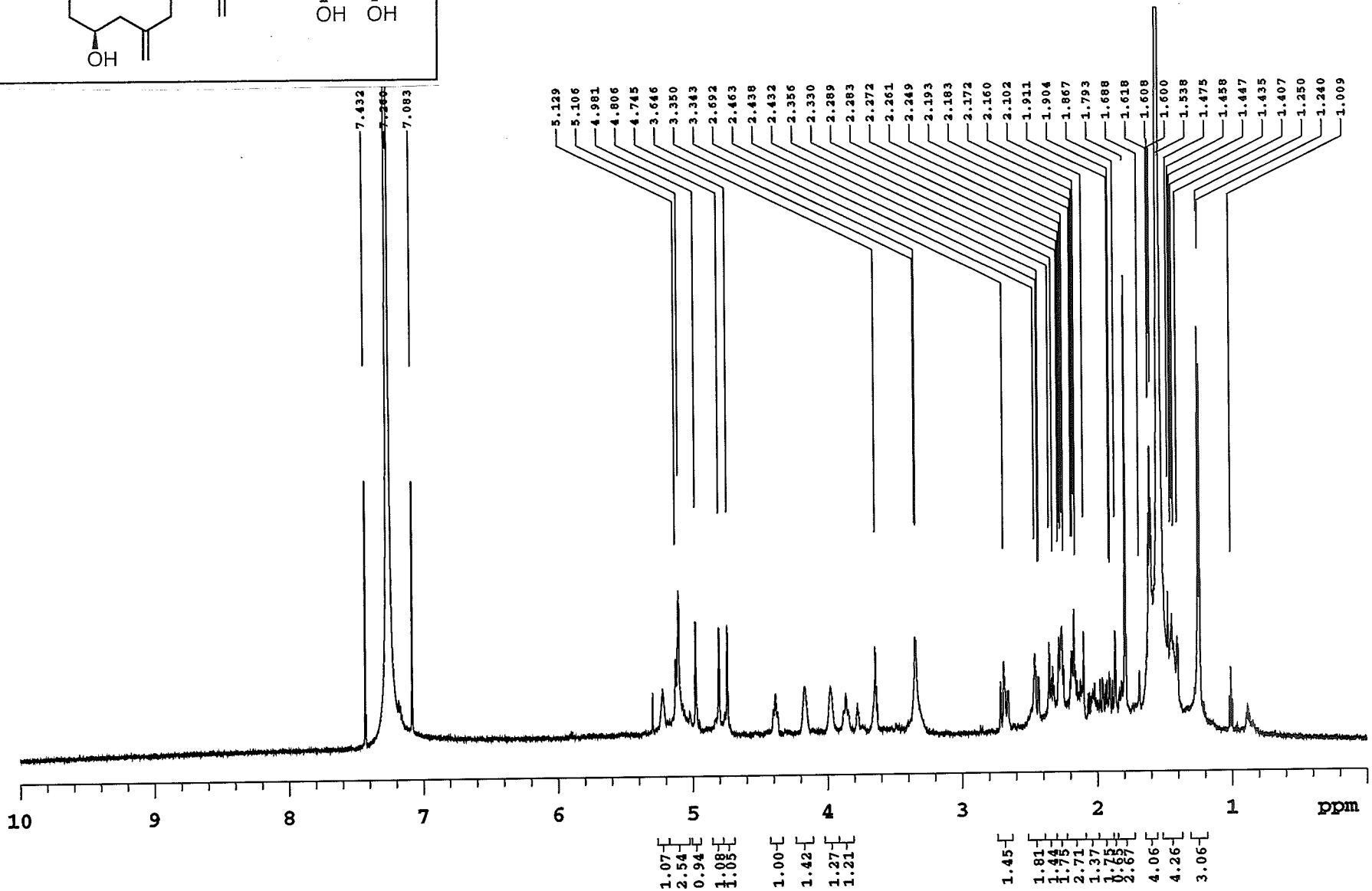
1.140
1.128
1.036
1.021
1.006
0.885
0.877
0.865
0.849
0.069
0.061
0.054
0.039
0.031
0.022
0.015
-0.001
0.70
0.74
0.69
0.72
0.69
1.86
1.00
1.32
2.79
1.97
2.88
2.81
0.79
0.55
2.72
3.24
2.75
4.10
2.95
36.34
23.24
9
8
7
6
5
4
3
2
1
0
ppm


TBSO
O
Me
O
Me
TBSO
OTBS
TBSO
172.337
145.710
141.941
132.961
130.727
127.995
117.531
111.958
77.202
76.992
76.781
71.680
71.157
70.027
69.243
68.147
66.359
47.978
46.663
43.467
39.715
39.125
38.155
37.430
35.946
34.833
29.690
25.929
25.887
25.862
25.820
24.487
23.113
21.857
21.292
20.103
18.703
18.189
18.155
18.138
18.096
-3.902
-4.071
-4.214
-4.290
-4.357
-4.391
-4.467
-4.669
-4.771
180
160
140
120
100
80
60
40
20
0
ppm


HO
O
Me
O
Me
OH
OH
OH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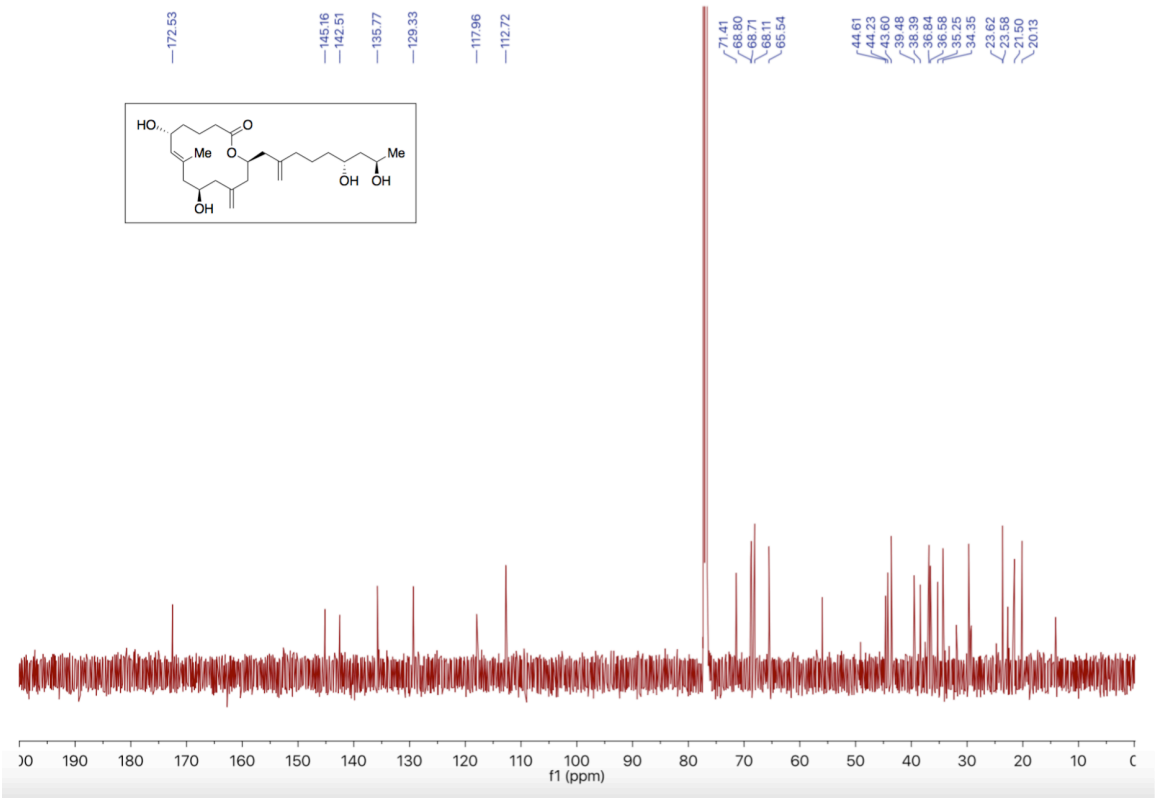
7.265
7.083
5.129
5.106
4.981
4.806
4.745
3.646
3.350
3.343
2.692
2.463
2.438
2.432
2.356
2.330
2.289
2.283
2.272
2.261
2.249
2.193
2.183
2.172
2.160
2.102
1.911
1.904
1.867
1.793
1.688
1.618
1.608
1.600
1.538
1.475
1.458
1.447
1.435
1.407
1.250
1.240
1.009
10
9
8
7
6
5
4
3
2
1
ppm
1.07
2.54
0.94
1.08
1.05
1.00
1.42
1.27
1.21
1.45
1.81
1.44
1.75
2.71
1.37
1.75
0.69
2.67
4.06
4.26
3.06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145.16
142.51
135.77
129.33
117.96
112.72
71.41
68.80
68.71
68.11
65.54
44.61
44.23
43.60
39.48
38.39
36.84
36.58
35.25
34.35
23.62
23.58
21.50
20.13
HO
O
Me
O
Me
OH
OH
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)